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TITLE: Effects of Early Acute Care on Autonomic Outcomes in SCI: Bedside to Bench and Back

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14. ABSTRACT Early management of blood pressure (BP) may be critical to outcome after spinal cord injury (SCI), but evidence-based protocols are needed. Optimal early treatment and management of SCI has not been established in clinical practice, nor in animal models. Guidelines for management of BP in acute SCI have been influenced by the rather clear evidence of a relationship between hypotension and poor outcomes in TBI, and the aim of maintaining cerebral blood flow in the face of increased intracranial pressure (ICP), but doubt remains about what is best for SCI. This grant focuses on the following two hypotheses: <i>1) Episodes of low BP (measured by mean arterial pressure (MAP) and systolic BP) in the early management of clinical SCI predict worse long-term functional outcomes, and 2) spontaneous hypotensive episodes in the perioperative period of experimental SCI in rats will result in worse outcomes.</i> Both clinical data and experimental modeling studies address these specific hypotheses.					
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Progress Report – Year 2

Award Number: W81XWH-13-1-0297

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Project Title: Effects of Early Acute Care on Autonomic Outcomes in SCI: Bedside to Bench and Back

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Report Date: Oct 30, 2015

Report Period: Oct 1, 2014- Sept 30, 2015

Grants Officer's Representative : Ms. Jessica Clement

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Accomplishments

1. UCSF Animal Protocol and ACURO Protocol approvals were received.
2. Human Subjects Protocol approval letters for the retrospective study were received from SFGH, Santa Clara Valley Medical Center and Palo Alto VA Health Sciences Center were approved.
3. Human subjects protocol approvals for the prospective study at UCSF have been obtained and submitted to the DoD for approval. Additional information was requested and has now been supplied, and we are waiting for final approval to begin patient enrollment.
4. Established 1) surgical methods for implanting Data Sciences blood pressure transducers in rats, and 2) the drug delivery techniques using phenylephrine, dopamine, and norepinephrine to determine infusion rate, method of delivery, concentration, etc. for holding blood pressure (BP) at specified levels for 4 hours after SCI. We have obtained data on two sets of rats sustaining either a 200, or a 250 kilodyne impact at T3. BP, heart rate (HR), bladder function and locomotor function was then assessed for 4-6 weeks after injury.
5. Held meetings with SFGH clinicians to work on analyzing data from SFGH patient records for the retrospective study. We were able to access the large existing database containing q 1min BP data from SFGH SCI patients from 2007-2013. This analysis showed that patients with more epochs of hypotension had poorer outcome. A manuscript describing this was published in Journal of Neurotrauma this year (Hawryluk GWH, Whetstone W, Saigal R, Ferguson AR, Talbott JF, Bresnahan JC, Dhall SS, Pan J, Beattie MS, Manley GT (2015) Mean arterial blood pressures and duration of hypotension correlate with neurological recovery following

human spinal cord injury: Analysis of high frequency physiologic data. *J. Neurotrauma*, online ahead of print; (doi: 10.1089/neu.2014.3778)).

6. Once access to the SCI patient data was established, we were able to evaluate MRI records as well. In collaboration with Dr. Jason Talbott of the Department of Radiology, this data was used to establish a new MRI scoring system for SCI that was then correlated with change in outcome. The scoring method was evaluated for inter-rater reliability and for predictive value related to general function as reflected by the AIS grade. A paper describing the system and its application to the cervical cord was published this year (Talbott JF, Whetstone W, Ready W, Ferguson AR, Bresnahan JC, Saigal R, Hawlryluk GWH, Beattie MS, Mabray M, Pan J, Manley GT, Dhall SS. (2015) The Brain and Spinal Injury Center (BASIC) spinal cord injury (SCI) score: A novel, simple, and reproducible method for assessing severity of acute cervical SCI using axial T2 MRI. *J.Neurosurgery (Spine)*, 2015, 23:495-504; <http://thejns.org/doi/abs/10.3171/2015.1.SPINE141033>). And a second paper applying the method to thoracic injury patients is now in press (Mabray MC, Talbott JF, Whetstone WD, Dhall SS, Phillips DB, Pan JZ, Manley GT, Bresnahan JC, Beattie MS, Haefeli J, Ferguson AR. Multidimensional analysis of MRI predicts outcome in thoracic and thoracolumbar spinal cord injury. (2015) *J Neurotrauma*, in press; doi: 10.1089/neu.2015.4093).
7. The retrospective analysis also was used to identify complications and outcomes of vasopressor usage in central cord syndrome and a paper describing these results has been accepted for publication (Readdy WJ, Whetstone W, , Ferguson AR, Talbott JF, Inoue T, Saigal R, Bresnahan JC, Beattie MS, Pan J, Manley GT, Dhall SS (2015) Complications and outcomes of vasopressor usage in acute traumatic central cord syndrome. *J. Neurosurgery (Spine)*, in press; <http://thejns.org/doi/abs/10.3171/2015.2.SPINE14746>).
8. We have also developed novel methods for analyzing the large body of retrospective laboratory SCI data in the Beattie/Bresnahan Laboratory. In one such query, we were able to identify a relationship between high blood pressure at the time of injury and poor neurological recovery. This information has just been published in *Nature Communications* (Nielson, J, Paquette J, Liu AW, Guandique CF, Inoue T, Irvine KA, Gensel JG, Petrossian TC, Lum PY, Carlsson GE, Manley GT, Beattie MS, Bresnahan JC, Ferguson AR. Big-data visualization for translational neurotrauma. Topological data analysis for discovery in preclinical spinal cord injury and traumatic brain injury. *Nature Communications*, 2015, 6:8581).
9. We held meetings with Drs. Creasey and McKenna and we have identified procedures for accessing data from Santa Clara Valley Medical Center and Palo Alto VA Health Sciences Center. A database structure and a data dictionary was developed at SFGH first for the retrospective studies, and now for the prospective study data collection (REDCap). This database

has now been transferred to Santa Clara and to the PA VA to use on their retrospective data, and data is now being entered.

Reportable Outcomes/ Specific Aims and Major tasks

Major Task 1: Regulatory set up for animal and human studies (Specific aims 1-3)

Subtask 1: UCSF Retrospective study IRB approval

UCSF IRB approval for retrospective chart review for this project was obtained and has been approved by the DoD.

Subtask 2: UCSF IACUC approval

The UCSF IACUC approval was obtained and then ACURO and approval was received.

Subtask 3: PAVAHCS and SCVMC retrospective study IRB approvals

The VA SCVMC approvals have been completed, and the subcontracts for these organizations have been finalized and approved by the DoD.

Subtask 4: SFGH Prospective study: Consent forms, IRB approval

The protocol for the prospective study is currently pending approval. The initial research protocol application and supportive documents were submitted and received by the DoD on August 4, 2015. The UCSF team received a request for revisions September 22, 2015 which included a request for local IRB application modifications. Completed DoD revisions were submitted October 20, 2015 after IRB applications were approved by the UCSF Committee of Human Research (CHR). Biosketches for Principal Investigator/Associate Investigators and human subjects protection training certifications were also sent over at that time. An additional DoD request was sent to the UCSF team on October 21, 2015 regarding medical record release language in the Informed Consent Form. The UCSF team is currently waiting for CHR approval for the consent modification prior to DoD re-submission.

The continuation for an additional year of the retrospective study was submitted for review on October 22, 2015.

Milestone(s) Achieved: Animal and retrospective study approvals obtained.

Specific Aim 1: Examine the available evidence for a correlation between early BP (and bladder/bowel) management, vasopressor use, and later outcomes, including outcomes on autonomic, bladder and bowel function. (year 1-2)

Major Task 1:

Retrospective review of paper and electronic medical records of SCI patients.

Subtasks 1-4: We have established a database for entry of retrospective data, first using SFGH data. We have included the NINDS SCI CDEs. A short version of this database is attached as Appendix 1. A data dictionary has been established and the database has been transferred to the two other sites (SCVMC and the PAVAMC). Data collection in a HIPA compliant fashion at those sites is underway using retrospectively identified SCI patients records.

SPINAL CORD INJURY REDCAP DATABASE

Redcap Data Dictionary

Total Variables Collected

As of 10/05/2015: 1,294 Variables

NINDS Common Data Element (CDE) Count

Core-CDE: 199 Variables

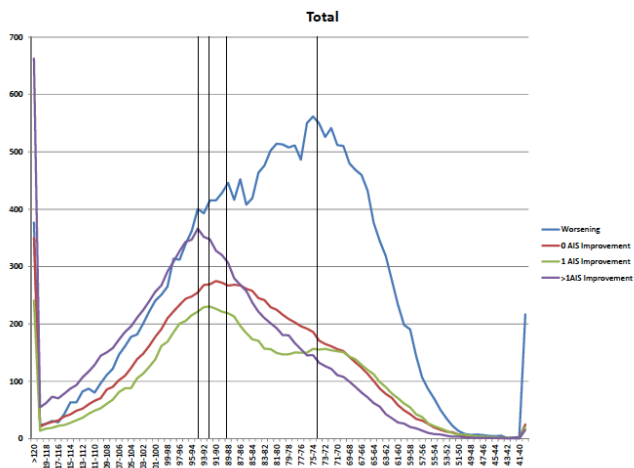
Supplementary-CDE: 642 Variables

Exploratory-CDE: 43 Variables

Major Task 2:

Retrospective review of paper and electronic medical records of SCI patients

We have held meetings with the SFGH spinal cord injury clinicians and have established methods for accessing a large dataset collected over the past several years from the ICU using the Aristein monitoring system which contains q 1min blood pressure data for all



SCI patients during their ICU stay.

Data were loaded into the HIPA compliant database 'REDCap' for querying. Dr. Whetstone has already organized other data from most of these SCI patients treated at SFGH; this data has been matched to the data in the Aristein monitoring system by Dr. Gregory Hawryluk who was able to access the BP data using Matlab programs that he wrote. We have analyzed the q 1 min data on physiological monitoring of all SCI patients seen

between 2005 and 2011 and compared it to the ASIA grade status over the ICU stay. The data show that patients with more epochs of low BP show worsening AIS motor scores (from Hawryluk et al., 2015). This first analysis was presented at the National Neurotrauma Society meetings in San Francisco on June 30, 2014. The advantage of these data is that it doesn't only show average MAPs but shows every instance of low blood pressure during the entire recording period from admission to discharge in the ICU. There was a significant relationship between the number of epochs of MAP below 80 and poorer outcome at discharge from the ICU providing initial support for the hypothesis driving this grant. This paper has been published online in the Journal of Neurotrauma.

Other data to come out of the retrospective analysis from the patients at SFGH include the following:

1) Vasopressor usage in acute traumatic central cord syndrome (ATCCS) patients is associated with complication rates that are similar to the reported literature for SCI. Dopamine was associated with a higher risk of complications in patients > 55 years. Given the increased incidence of ATCCS in older populations, determination of MAP goals and vasopressor administration should be carefully considered in these patients. While a randomized control trial on this topic may not be practical, a multiinstitutional prospective study for SCI that includes ATCCS patients as a subpopulation would be useful for examining MAP goals in this population. These results are reported in a manuscript in J Neurosurgery (Spine) by Readdy et al, (2015).

2) The Brain and Spinal Injury Center score was developed to categorize the T2-weighted MRIs of spinal cord injured patients in the database. A simple categorical scale was developed and validated. The BASIC score strongly correlated with neurological symptoms at the time of both hospital admission and discharge. It also distinguished patients initially presenting with complete injury who improved by at least one AIS grade by the time of discharge from those whose injury did not improve. The BASIC score was rapid to apply and showed excellent interrater reliability. The new score improves on current MRI-based prognostic descriptions for SCI by reflecting functionally and anatomically significant patterns of intramedullary T2 signal abnormality in the axial plane. This score was published this July in the Journal of Neurosurgery (Spine) (Talbot et al, 2015), and a second paper applying the method to thoracic SCI is in press at The Journal of Neurotrauma (Mabray et al., 2015). For this second paper, advanced analytic methods using multivariate principle components analysis showed that the BASIC score was the only statistically significant predictor of Asia Impairment Grade at discharge as compared to other current methods of imaging assessment of SCI. The study provides evidence of convergent validity, construct validity, and clinical predictive validity for the sampled MRI measures of SCI when applied in acute thoracic and thoracolumbar SCI.

Specific Aim 2: Provide detailed reports and physiological monitoring in the pre-hospital, ED and ICU to identify cardiovascular parameters and (events) during early management of SCI that are associated with poor outcome, including bowel and bladder function.

Major Task 4: Perform detailed physiological monitoring in the ED and ICU for 1st 7 days after SCI.

Subtask 1: Use prior SCI+TBI and early results of consortium BP record evaluations to finalize data collection strategy for prospective study.

We have currently set up the RedCap database and have finalized the data entry forms for the prospective study based on our retrospective analyses.

Subtask 2: Train and coordinate investigators and clinical staff in ED, ICU, and rehab. New members have been added to the SFGH/UCSF group to participate as clinical investigators including Sanjay Dhall, MD, Neurosurgery, Jason Talbot MD, PhD Radiology, Jonathan Pan MD, PhD, Anesthesiology, will join co-investigators William Whetstone MD from Emergency Medicine and Geoffrey Manley MD, PhD who are already on the project. This team has worked together on the retrospective study and has a good working relationship already established as we move forward for the prospective study. A related but separate prospective study entitled “Canadian Multicentre CSF Monitoring and Biomarker Study” CAMPER is just starting as well. The Rick Hansen Institute sent trainers to train and certify our clinical coordinators and nurse-practitioners to perform ASIA sensory and motor scoring. We will be sharing clinical coordinators with the large prospective observational study TRACK-TBI which will allow us, with limited funds, to cover 24/7 enrollment of SCI patients. The human subjects protocols are awaiting final approval to begin.

Subtask 3: Begin accrual. This will begin shortly.

Specific Aim 3: Determine the effects of episodes of hypotension and hypertension on the recovery of locomotor and bladder and bowel function in our rat model of high thoracic contusion SCI. We will examine the effects of commonly used vasopressors on outcome.

Major Task 5: Establish methods for BP regulation using the proposed hypo- and hypertensive treatments in the high thoracic injury model.

Subtask 1: Consult with clinical investigators to appropriately model the cardiovascular manipulations in the animal study.

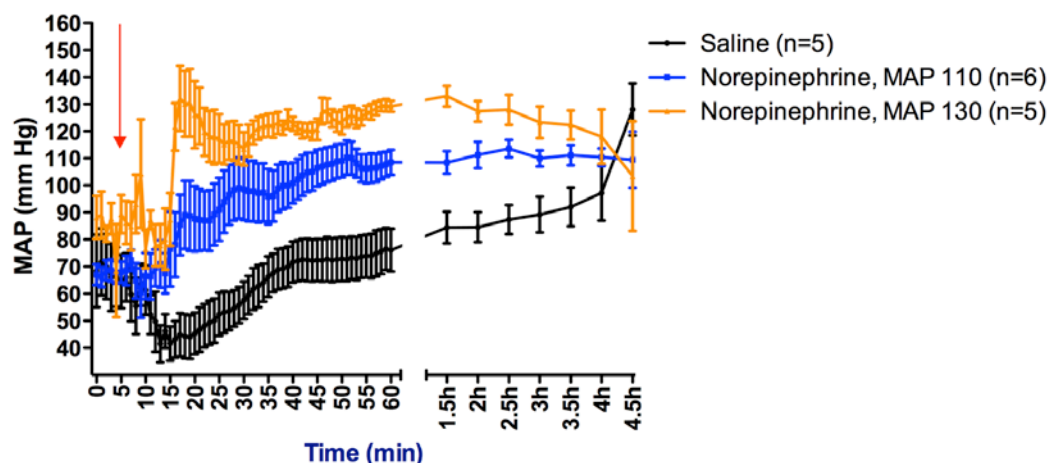
We have enlisted the participation of Dr. Jonathan Pan MD, PhD of the Anesthesia Department who has training in SCI research, to help with this aspect of the project.

Subtask 2. Perform control study in rats with high thoracic SCI to determine appropriate drug and dosing for hypo- and hypertensive treatments. After considerable effort and testing of various methods, we are now able to control the BP of rat patients for 4 hours after SCI.

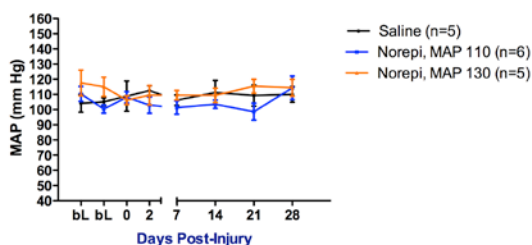
Major Task 6: Perform high thoracic, moderate-severe SCI in cohorts of rats and monitor BP, bladder and bowel functional measures, and locomotor function over 4-6 weeks. Groups include a) control group - no manipulation or treatments; b) group with MAP maintained at 75 with dopamine; c) group with BP maintained at 90 mm Hg using pressors; d) hypertensive group – BP maintained at 120 mm Hg induced with pressors.

We have tested the effect of 200 and 250 kilodyne impacts using the Infinite Horizons contusion device at T3, on recovery in groups of rats with their blood pressure maintained at different levels after injury. The data reported below are for the groups receiving 250kdyne injuries at T3. After much experimentation, we were

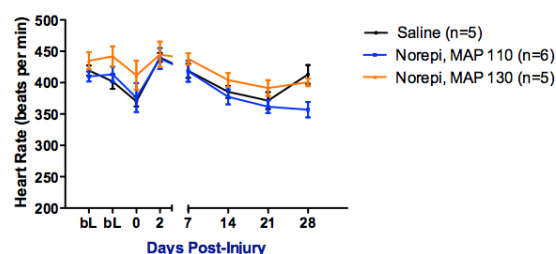
Cardiovascular maintenance immediately post-SCI for 4hrs



MAP over 4 weeks

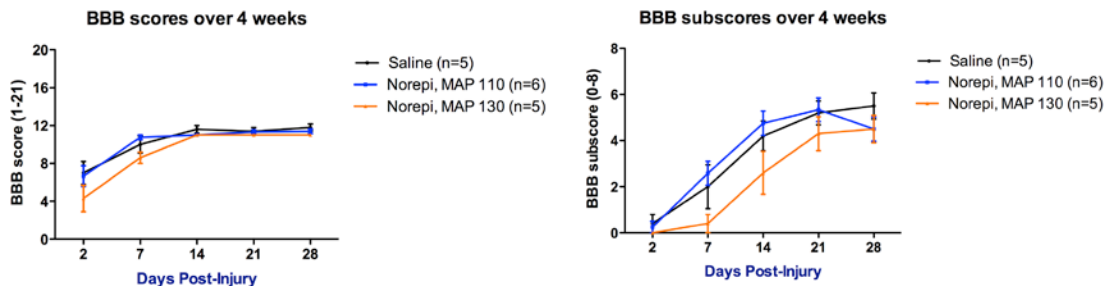


Heart Rate over 4 weeks



able to maintain BP using NE in combination with the anesthetic isoflurane. We then recorded cardiovascular function over 4 weeks and that data is shown below.

After initial BP intervention with norepinephrine for 4 hours, animal BPs were able to return to their baselines. There is significant difference in MAP values for 4 weeks between groups of NE 110 and NE 130 (One Way ANOVA with repeated measures, $p < 0.05$). Normal HR values vary from 350 – 450 bpm. At the time of injury, HR acutely dropped 50 - 100bpm, and gradually recovered over the first week. Over the following 3 weeks, rat HR slowly declined and stabilized. Both saline and NE 110 groups have a significantly lower heart rate than NE 130 (One way ANOVA repeated measures were $p < 0.05$). Locomotor recovery was also measured over 4 weeks after SCI and the data shown below, indicated no significant difference between groups on the overall BBB scores. Analysis of BBB-subscores revealed the following: compared to the saline group, the NE 110 group had similar functional recovery over time (One way ANOVA repeated measures, no significance); NE 130 group had delayed recovery and persistent lower sub-scores during 4 week recovery (One way



ANOVA repeated measures $p < 0.05$ for both comparisons i.e. NE 130 vs. NE 110 and NE 130 vs. Saline). These data suggest that the high BP group had poorer outcome.

A number of micturition outcomes were also taken for these groups of rats without clear significant differences between groups. We are in the process of filling in these groups and will report on the full complement in the next progress report. Given the huge amount of data that we have gathered on these subjects, we will also use multivariate analytic methods to give us an idea of the factors that are varying together.

As an additional approach to trying to understand the autonomic outcome measures, we have queried the extensive historical data available in the Beattie/Bresnahan laboratory to identify predictors of poor outcome after SCI in the rat. This data was entered into a large dataset overseen by Dr. Adam Ferguson (the VISION-SCI database) and Dr. Jessica Nielsen, in an independent query of this large dataset, identified a group of animals with poor outcome all of whom had high BP at the time of surgery (Nielsen et al, 2015). This data correlates with the above described data and indicates that high blood pressure is also a negative predictor of outcome. We are now analyzing the human data to determine if this can also be seen in the SCI patients. At the current time, we have identified very high MAP in a subset of patients during surgery and will attempt to do a similar analysis with these

patients. Certainly, in the TBI literature, both very high and very low BP predict poorer outcome and likely the same will hold true for SCI.

Subcontract sites report:

Prepared by Dr. Stephen McKenna (Santa Clara Valley Medical Center) and Dr. Graham Creasey (VA Palo Alto Health Care System)

Major Task 1: Regulatory set up for animal and human studies (Specific aims

1-3) Subtask 3: PAVAHCS and SCVMC retrospective study IRB approvals

- i. Regulatory compliance has been maintained with the SCVMC IRB and the Stanford IRB.
- ii. Regulatory approval is being obtained for data sharing between sites using a common database described below, while maintaining the privacy and confidentiality of Protected Health Information.

Specific Aim 1: Examine the available evidence for a correlation between early BP (and bladder/bowel) management, vasopressor use, and later outcomes, including outcomes on autonomic, bladder and bowel function. (year 1-2)

Completed in Year 1. There was very little existing information about a correlation between early management and later outcomes for autonomic, bladder and bowel function. We have therefore engaged on the data collection activities described below.

Major Task 2: Review of paper and electronic medical records of SCI patients

Data collection and analysis is in progress using medical and urodynamic records of patients in the SCI Units. 778 veterans are on active follow-up in the VA SCI Unit and their bladder management and urodynamic evaluations are being analyzed. A paper entitled “Upper Urinary Tract Imaging and Assessment in a Cohort of Veterans with Spinal Cord Injuries or Disorders” has been accepted for platform presentation by Dr. Sophia Miryam Schussler-Fiorenza Rose, our Advanced SCI Fellow, at the annual conference of the Association of Academic Physiatrists in 2015.

Subtask 1: Develop SCI Consortium (SCIC) data dictionary and coding manual to include the following:

- *Conformance with NINDS SCI CDEs*
- *Additional locally defined elements pertinent to the SCIC project aims*
- *Rules and error flags for data field ranges, relational consistency and completeness*
- *Measures to safeguard research subject confidential information through elimination of any identifying PHI.*

In order to develop the SCIC data dictionary and coding manual, the following major activities have been undertaken:

1. Bi-weekly TrackSCI team meetings have been held to co-ordinate efforts between sites
2. Form Review at VA and SCVMC indicated that there were no consistent forms being used to document autonomic outcomes. We have been developing a data dictionary and RedCap database using NIH Common Data Elements and

International SCI Data Sets to facilitate collection of this data between the three sites of our Translational Research Partnership.

3. Collaboration with national and international initiatives to harmonize SCI data sets.

- i. A meeting of approximately 20 representatives of SCI registries and databases was organized at the combined conference of the American Spinal Injuries Association and the International Spinal Cord Society in Montreal in May 2015, in order to plan an international initiative to compare, harmonize and potentially combine SCI data.
- ii. We participated in the organization of a Workshop held at the National Institutes of Health in 2015 to create an International Spinal Data Network. The workshop was attended by representatives of the National Spinal Cord Injury Statistical Center representing the US Model SCI Systems, the VA System of Care for Spinal Cord Injuries and Disorders, the North American Clinical Trial Network, the Rick Hansen Institute Spinal Cord Injury Registry, and the European Multicenter Study of Spinal Cord Injury, and was sponsored by the Rick Hansen Institute (Canada), the Craig Neilsen Foundation (USA) and Wings for Life (Europe). The Network was formed and agreed to begin an international comparison and verification of the data elements in the SCI registries and databases maintained by the participants.
- iii. All of our three sites have been visited by and have collaborated with Prof. Fin Biering-Sorensen of Copenhagen, Denmark, Past President of the International Spinal Cord Injury Society, who has obtained agreement for the inclusion of the International SCI Data Sets into the EPIC electronic medical record which is used at the Santa Clara Valley Medical System
- iv. We are collaborating with Dr. Sophia Chun, the newly appointed leader of the VA System of Care for Spinal Cord Injuries and Disorders, to develop a new VA database for spinal cord injuries and outcomes integrated with the VA Computerized Patient Record System, the electronic medical record that has been in use for nearly two decades.

4. Participation in the separate but related Canadian Multicentre CSF Monitoring and Biomarker Study (CAMPER). This will

- i. Measure the pressure in the cerebrospinal spinal fluid below an acute spinal cord lesion in humans via an indwelling lumbar catheter and compare this with the Mean Arterial Pressure to determine the Spinal Cord Perfusion Pressure.
- ii. Determine how vasopressors, which are used to control blood pressure following SCI, influence cerebrospinal fluid pressure.
- iii. Characterize the severity of an SCI using the levels of specific protein biomarkers within the cerebrospinal fluid.
- iv. Correlate neurologic recovery with the levels of specific proteins biomarkers within the cerebrospinal fluid.

Subtask 2: Design the SCIC database and electronic Case Report Forms (eCRFs) on a shared platform for SFGH, SCVMC and VAPAHCS and training of data collectors at all 3 sites on abstraction of retrospective data.

- i. The SCIC database and eCRFs have been developed
- ii. Data collectors have been trained
- iii. Data collection is proceeding at Santa Clara Valley Medical Center
- iv. Permission for inclusion of data from the VA Palo Alto Health Care System is awaited.

Subtask 3: Mapping and migration of existing retroactive patient data sets from SCVMC and SFGH to SCIC database.

Mapping and migration of retroactive patient data is in progress as described above.

Subtask 4: Initiate data collection for retrospective SCI cases for 2005-2015.

- i. Collection and analysis of urological data for SCI patients in VA databases and urodynamic records is in progress as described above.
- ii. In conjunction with the EPIC electronic medical record IT team, tools for retrospective data collection are in development at SCVMC.

Major Task 3: Analyze records of early management (BP and bladder/bowel management including urodynamics), and conduct automated text mining of electronic medical records and medication administration. Identify potential outcomes that do not conform and that may be emerging CDEs.

The format of records of early blood pressure, bowel and bladder function, and urodynamics have been analyzed in preparation for text mining of medical records. Many records do not conform to existing standards and are being revised to be compatible with the International Standards to Document Remaining Autonomic Function after Spinal Cord Injury, the NIH Common Data Elements and the International SCI Data Sets.

Major Task 4: Perform detailed physiological monitoring in the ED and ICU for 1st 7 days after SCI.

Subtask 1: Use prior SCI+TBI and early results of consortium BP record evaluations to finalize data collection strategy for prospective study.

- i. Data on veterans with concurrent TBI and traumatic SCI occurring from 1952 to 2012 and undergoing lifetime follow-up in the SCI Unit of the VA Palo Alto has been abstracted from unstructured text in the VA Computerized Patient Record System to test a data collection strategy and to determine the information available. A journal article has been accepted for publication as follows:

Creasey GH, Lateva Z, Schussler-Fiorenza Rose SM, and Rose J. Traumatic brain injury in US veterans with traumatic spinal cord injury. J Rehabil Res Dev 2015;52(6):669-76

Major Task 5: Establish methods for BP regulation using the proposed hypo- and hypertensive treatments in the high thoracic injury model.

See UCSF report above.

Major Task 6: Perform high thoracic, moderate-severe SCI in cohorts of rats and monitor BP, bladder and bowel functional measures, and locomotor

function over 6 weeks. Groups will include a) control group - no manipulation or treatments; b) group with MAP maintained at 75 with dopamine; c) group with BP maintained at 90 mm Hg using pressors; d) hypertensive group – BP maintained at 120 mm Hg induced with pressors.

See UCSF report above.

Santa Clara Valley Site: Stephen McKenna, MD, subcontract site PI

IRB approval at SCVMC has been obtained to upload de-identified autonomic data into a UCSF hosted REDCAP database. In addition, REDCAP data dictionaries have been built based on the findings of our TrackSCI partnership, to upload CDE based autonomic data while maintaining the privacy and confidentiality of Protected Health Information. The eventual goal is to create a REDCAP database to combine autonomic OR data across multiple facilities.

Currently the team has identified 21 patients with traumatic SCI who have undergone surgery and subsequent rehabilitation at SCVMC to be used for retrospective data collection. The data collection process was initiated by comparing variables contained in the SCVMC OR records to those in the SFGH OR records to identify common variables, and also to determine whether these variables correspond to the Common Data Elements of the NINDS.

UCSF Research Assistants have met with SCVMC and VA staff to begin initial set-up of multi-center Redcap database for traumatic SCI data collection.

We have discussed the possibility of collecting autonomic OR data from SCVMC based on findings from SFGH on the prevalence of hypertension during surgery following traumatic SCI. Replicating this project at SCVMC would provide insight into long-term functional rehabilitation outcomes to determine whether autonomic changes during surgery impact functional recovery following traumatic SCI.

We are currently manually extracting autonomic data as well as information regarding vasopressors and anesthetics delivered throughout the surgery from SCVMC OR records. Data from 4 out of the 21 records have currently been collected. We developed a preliminary database in a secure excel file format on the SCVMC network that can be easily transferred into the Redcap database.

UCSF research assistants met with an anesthesiologist at SCVMC for clarification on variables of interest including autonomic data and drug dosing throughout surgery. We discussed the possibility of obtaining read-only access to electronic OR records that contain digitized autonomic data which would significantly expedite the data collection process. We identified location of functional outcome variables including ISNCSCI and FIM scores in EMR. We need to determine whether pre-operative ISNCSCI scores are routinely collected.

In order to facilitate surgical autonomic data collection, we are pursuing the use of read-only access for OR record. These data are being matched to functional outcomes including pre-operative, post-operative, and discharge ISNCSCI scores as well as FIM scores throughout rehabilitation. Variables of interest coincide with the Common Data Elements defined by the NINDS. The goal in collecting this data is to characterize periods of hypo and hypertension during surgery, the degree to which MAP goals are achieved, and the impact of autonomic fluctuations during surgery on functional outcomes after traumatic SCI.

In addition, a sub analysis has been conducted using Principal Component Analysis on early respiratory autonomic function. We conducted a retrospective chart analysis of all consecutively admitted SCI patients to SCVMC's Rehabilitation Trauma Center from May 2013 to January 2015. We included all spinal cord injured patients with: neurologic level of injury between C1 and C5, American Spinal Cord Injury Association (ASIA) grade A or B, date of injury within 3 months of admission, history of tracheostomy, and ventilator dependence. We recorded respiratory autonomic data including daily forced vital capacity (FVC) checks, daily ventilator-free breathing progress, ventilator settings, and pulmonary co-morbidities from each patient's past medical history. Data was de-identified via the Safe Harbor method and uploaded to the TrackSCI REDCAP database at San Francisco General Hospital for analysis. We are preparing a manuscript using Principal Component Analysis to identify multifactorial predictors of CDE based respiratory autonomic outcomes.



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Traumatic brain injury in U.S. Veterans with traumatic spinal cord injury

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Abstract — Patients with both a spinal cord injury (SCI) and traumatic brain injury (TBI) are often very difficult to manage and can strain the resources of clinical units specialized in treating either diagnosis. However, a wide range of estimates exists on the extent of this problem. The aim of this study was to describe the scope of the problem in a well-defined population attending a comprehensive SCI unit. Electronic medical records of all patients with SCI being followed by the SCI unit in a U.S. Veterans' hospital were searched to identify those with concurrent TBI. The data were analyzed for age, sex, cause of injury, level and completeness of SCI, cognitive impairment, relationship with Active Duty military, and date of injury. Of 409 Veterans with a traumatic SCI, 99 (24.2%) were identified as having had a concurrent TBI. The occurrence did not appear to be closely related to military conflict. Reports of TBI were much more common in the last 20 yr than in previous decades. Documentation of TBI in patients with SCI was inconsistent. Improved screening and documentation could identify all patients with this dual diagnosis and facilitate appropriate management.

Key words: Active Duty military, cognitive impairment, electronic medical records, military trauma, polytrauma, retrospective study, spinal cord injury, traumatic brain injury, Veterans, Veterans Health Administration.

Abbreviations: CPRS = Computerized Patient Record System, ICD-9-CM = International Classification of Diseases-9th Revision-Clinical Modification, SCI = spinal cord injury, TBI = traumatic brain injury, VA = Department of Veterans Affairs.

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INTRODUCTION

Since World War II, when patients with spinal cord injury (SCI) began to survive in significant numbers, it has been recognized that SCI is often associated with other injuries. Recent military conflicts have drawn renewed attention to traumatic brain injury (TBI) and SCI [1–2]. Both can be catastrophic, and their management is particularly difficult when they occur in the same individual. Patients with paraplegia and co-occurring severe TBI have been shown to have worse motor outcomes and longer acute rehabilitation lengths of stay than those with paraplegia and no TBI [3]. There is, however, a wide range of estimates of the prevalence of such a dual diagnosis [4].

The prevalence of SCI among patients with TBI is relatively low. Two decades ago, acute spinal cord trauma was estimated to occur in between 5 and 15 percent of patients with severe head injury [5–6]. A recent article on closed or penetrating head injury sustained in military personnel in Iraq reported a 9.8 percent incidence of SCI or spinal column injury [7]. A retrospective study of 447 patients with moderate or severe head injury evaluated at two civilian level 1 trauma centers showed that 3.1 percent sustained SCI [8]. A prospective study of 180 patients with moderate or severe TBI admitted to a neurotrauma intensive care unit found that 7.8 percent had SCI [9].

The prevalence of TBI among patients with SCI is not clear and has a wide range of estimates. The Spinal Cord Injury Model Systems reported retrospectively in 1995 that 28.2 percent of patients with SCI had at least a mild TBI with loss of consciousness and 11.5 percent had a TBI severe enough to demonstrate cognitive or behavioral changes [10]. A more recent prospective study of a sample of 198 patients with SCI in a single large SCI model system estimated that 60 percent had TBI [4]. There may be several reasons for uncertainty about the prevalence of TBI in patients with SCI. The location of the study (e.g., trauma service, intensive care unit, SCI unit) and whether the injuries occurred in a

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military or civilian context will determine the population studied. Much depends on the design of the study and definitions used for TBI, particularly mild TBI whose definition has not always been clear and which can be confused with posttraumatic stress disorder and other conditions. Patients themselves may underreport TBI through lack of insight or a desire to return to Active Duty or overreport TBI in the context of compensation or to avoid the stigma of mental illness [11–13]. TBI may be particularly underdiagnosed in retrospective studies [14], where it is highly dependent on documentation.

In view of the wide range of published estimates and the medical, social, and financial significance of these injuries, we investigated documentation of TBI in a well-defined population with known SCI. The U.S. Department of Veterans Affairs (VA) has a national System of Care for Spinal Cord Injuries and Disorders, with 24 SCI centers and 127 SCI clinics arranged in a hub and spoke system. Veterans of the U.S. military with spinal cord injuries or disorders are accepted into this system for rehabilitation and lifetime follow-up, and their medical records are maintained in an electronic medical record known as the Computerized Patient Record System (CPRS). Most of the contents of this system are text-based, but they can be searched electronically, allowing for the examination of thousands of notes extending over many years.

METHODS

The SCI service of the VA Palo Alto Health Care System maintains a registry of patients with spinal cord injuries or disorders that undergo initial inpatient rehabilitation or follow-up care. Some of these patients sustained their SCI many years ago and continue to receive active follow-up at the SCI service as is recommended by the VA. The current study included patients who were admitted initially or for follow-up care during a 2 yr period (October 2010–October 2012). Patients who died during this period were not excluded. Since our interest was in co-occurrence of SCI and TBI, the first step was to identify the subset of patients with traumatic SCI. The etiology of traumatic SCI was determined using the Common Data Elements classification of (1) sports and leisure, (2) assault, (3) transport, (4) fall, and (5) other traumatic causes [15]. The Common Data Elements classification is based on the World Health Organization International Classification of External Causes of Injury and recommends that when the etiology is classifiable into more than one of these five categories, the category with the highest priority (the lowest number) should be assigned.

The personal identifiers of these patients were then used to obtain their electronic medical records in the VA CPRS and search for any reference to TBI or head injury. The electronic medical record of each patient includes a list of Active Problems, which uses codes of the International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM). The Active Problems list was examined and if a reference to TBI or head injury was found, the ICD-9-CM code was noted as well as the date of entry, which was used to determine whether the injury happened at the same time as the SCI. The electronic medical record may contain hundreds or even thousands of notes for each patient. The text of all notes was searched electronically for any of the following text phrases: "TBI," "brain injury," "brain trauma," "head injury," "head trauma," "loss of consciousness," or "LOC." When any of these words or phrases was found in the notes, their context was examined to determine whether the patient did indeed have a history of any TBI (mild, moderate, severe, or self-reported) and its relationship in time to the SCI. For patients identified as having TBI that occurred at the same time as SCI, an additional search for cognitive impairment was conducted. SCI service psychologists perform an annual evaluation of all patients. Every note from the SCI service psychologists includes a section on cognitive functioning that was identified by this search; each of these notes was then read to determine whether there was cognitive impairment and whether it was attributable to the TBI or to other known conditions. Other information was also extracted from the electronic medical record, such as sex, current age, age at the time of the SCI, date of SCI, and level and completeness of the spinal cord lesion. The military status (Active Duty or retired) of the Veteran at the time of the injury was also determined.

RESULTS

A total of 701 patients were included in this study, of whom 675 (96.3%) were male and 26 (3.7%) were female, which is typical in the Veteran population with SCI. Screening by cause of spinal cord or column damage revealed that 292 patients had nontraumatic damage and were excluded from further analysis. The remaining 409 (58%) patients had traumatic SCI, of whom only 9 were female. The mean \pm standard deviation current age of patients with traumatic SCI was 60 ± 13 yr (range: 23–98 yr) and the mean time since injury was 24 ± 16 yr (range: 1–69 yr).

Of the 409 patients with traumatic SCI, only 18 had any reference to TBI noted in their Active Problem list; in all these cases, the TBI had occurred at the same time as the SCI. However, electronic searching of the text of notes using the criteria described in the "Methods" section identified an additional 81 patients with traumatic SCI as having had a TBI at the same time as the SCI. Thus, a total of 99 out of 409 patients with traumatic SCI (24.2%) had experienced a concurrent TBI.

The Active Problems list in the CPRS thus did not record the existence of the TBI in over 80 percent of these cases. In many of these cases, the head and/or brain injury or trauma was also not mentioned in the history recorded on admission but only in the text of notes by psychologists working in the SCI service, sometimes when reviewing a patient years after the injury.

The available information was not sufficient to determine the severity of the TBI in each case. **Table 1** shows the distribution by sex and age group. **Table 1** also shows the distribution and frequencies by etiology of the traumatic SCI.

Transport (category 3) was the most common cause both in patients with SCI only (52%) and those with concurrent SCI and TBI (59%). Fall (category 4) was the second most common cause. Notably, when the SCI was caused by assault (category 2), concurrent TBI was rare. Of 47 cases with SCI due to assault, 39 were due to gunshot wounds and none of these 39 had concurrent TBI. The two cases with concurrent SCI and TBI due to assault were caused by shrapnel and rocket-propelled grenade, respectively. Thus, only 4 percent of all assault cases led to concurrent SCI and TBI compared with 26.8 percent of nonassault SCI etiologies.

Table 1.

Distribution and frequencies (%) of key patient characteristics by group: concurrent traumatic brain injury (TBI) and spinal cord injury (SCI), SCI only, and SCI total.

Characteristic	SCI + TBI (n = 99)	SCI Only (n = 310)	SCI Total (n = 409)
Sex			
Male	94 (95)	306 (99)	400 (98)
Female	5 (5)	4 (1)	9 (2)
Age (yr)			
20–39	17 (17)	20 (7)	37 (9)
40–59	37 (37)	97 (31)	134 (33)
≥60	45 (46)	193 (62)	238 (58)
Age at Time of SCI (yr)			
20–39	56 (57)	203 (65)	259 (63)
40–59	11 (11)	71 (23)	82 (20)
≥60	32 (32)	36 (12)	68 (17)
SCI Etiology			
Sports/Leisure	12 (12)	44 (14)	56 (14)
Assault	2 (2)	45 (14)	47 (11)
Transport	58 (59)	161 (52)	219 (54)
Fall	24 (24)	49 (16)	73 (18)
Other [*]	3 (3)	11 (4)	14 (3)
SCI Level and Completeness			
Complete Tetraplegia	9 (9)	55 (18)	64 (16)
Incomplete Tetraplegia	47 (48)	107 (34)	154 (38)
Complete Paraplegia	22 (22)	89 (29)	111 (27)
Incomplete Paraplegia	21 (21)	59 (19)	80 (19)

^{*}Other traumatic cases included patients struck by trees or other objects and construction and mining accidents (not falls).

The number of patients with cervical SCI was only slightly higher than the number with thoracic and lumbar SCI: 218 (53.3%) tetraplegia versus 191 (46.7%) paraplegia (Table 1). The frequencies of concurrent SCI and TBI among tetraplegia patients (25.7%) and among paraplegia patients (22.5%) were also similar.

About half of the patients with concurrent traumatic SCI and TBI were also found to have cognitive impairment: 54 out of 99 (55%). Further comments on this finding are given in the "Discussion" section.

Investigation of when the concurrent SCI and TBI occurred in relation to military service (Active Duty or after military discharge) revealed that most of the patients (69 [70%]) had been injured after leaving military duty. While 30 of the injuries occurred during Active Duty, the majority of cases (20) were caused by accidents during transport by road or air, 8 were caused by falls and sport or leisure activities, and only 2 were caused by assault (shrapnel or rocket-propelled grenade).

When patients were stratified according to the date of their traumatic SCI, it became notable that records of concurrent TBI had increased greatly in recent years (Table 2). Half of all patients for whom we found electronic medical records of concurrent SCI and TBI were injured in the last decade (2003 to 2012). For comparison, the cases with SCI were more evenly distributed (15% to 24%) between different decades. Possible reasons for this are discussed later.

Table 2.

Distribution and frequencies (%) of concurrent traumatic brain injury (TBI) and spinal cord injury (SCI), SCI only, and SCI total by date of injury.

Date of Injury	SCI + TBI (n = 99)	SCI Only (n = 310)	SCI Total (n = 409)
2003–2012	49 (50)	71 (23)	120 (29)
1993–2002	23 (23)	47 (15)	70 (17)
1983–1992	11 (11)	50 (16)	61 (15)
1973–1982	6 (6)	74 (24)	80 (20)
1963–1972	9 (9)	56 (18)	65 (16)
<1963	1 (1)	12 (4)	13 (3)

DISCUSSION

In this single-center retrospective study, the overall percentage of patients with traumatic SCI who were recorded as having had a concurrent TBI was 24.2 percent, and for nonassault etiologies the frequency was slightly higher (26.8%). This frequency is similar to multicenter retrospective figures from the SCI model systems reported in 1995 (28.2%) [10] but lower than figures from a prospective study in a single SCI model system reported in 2008 (60%) [4]. We believe that

the higher frequency found in the prospective research study is attributable to more accurate screening and documentation of associated injuries at the time of the SCI and that more consistent screening and documentation of associated injuries, particularly TBI, is required in clinical practice, as discussed later.

Some studies have found cervical SCI to be associated with greater rates of concurrent TBI [4,9]. Our results did not show significant differences in the frequency of TBI between the groups of patients with tetraplegia or paraplegia (**Table 1**).

In the current study, the number of Veterans with traumatic SCI in whom a concurrent TBI was recorded has increased substantially over recent decades, from <9 percent before 1983 to 50 percent since 2003, while the number of patients with SCI only stayed more or less similar over time (**Table 2**). Three possible reasons are discussed next.

Military Activity

In recent years, TBI has been described as the signature injury of military action in the Middle East, and it might be hypothesized that this has increased the number of patients with SCI and TBI. However, patients whose SCI was caused by gunshot wound or shrapnel were rarely recorded in this study as having a TBI, presumably because missiles strike either the spine or head but rarely both, and in recent conflicts the use of body armor appears to have greatly reduced the incidence of SCI. It is well known that during Active Duty, many injuries are caused not in combat but by other forms of trauma such as motor vehicle accidents. In this study, while 30 percent of concurrent injuries occurred during Active Duty, the majority of these occurred during transport by road or air. Only 7 of 99 concurrent injuries occurred during combat, and none were caused by a gunshot; one was caused by shrapnel, one by rocket-propelled grenade, two by motor vehicle accidents, and three by flying accidents. It seems likely, therefore, that the contribution of military combat to increasing records of concurrent SCI and TBI is small.

Improved Documentation

The CPRS was introduced by the VA in 1997. Patients injured before this time have their current medical records entered into this system, but the notes about their medical history before this time are often dependent on patients' memory, which can be impaired if they had a head injury or because of their current age. The CPRS provides improved ability to retrieve information entered about injuries since 1997. However, proper documentation also depends on whether patients are asked about the possibility of past head injury even if the injury resolved, which depends on awareness by clinical staff of the possibility of head injury.

Improved Awareness

Awareness of head injury in military personnel has increased during the last two decades, and this has led to increased screening in the Department of Defense and VA. Psychologists working in SCI units are usually aware of this, but other staff, including medical residents in training who may do much of the documentation, may be less aware of the possibility of head injury and less skilled in diagnosing it. The results of screening in the Department of Defense are not necessarily made available to the VA when a patient is transferred. We believe that more consistent documentation and communication of this information should become standard practice in the Department of Defense and VA to reduce the chance of missing a diagnosis of TBI.

Traumatic SCI usually has obvious symptoms and signs and is therefore relatively rarely missed, and major TBI is rarely missed as well. When both are present, management is usually assigned to either an SCI or TBI unit, depending on the relative severity of the two injuries. Ideally, the staff of such units would collaborate in the management of such patients. However, SCI and TBI units may not be located in the same institution, and even when they are, they often have different cultures and collaboration may be limited. In practice, each unit will concentrate on the injury it knows best, and the other injury may not receive state-of-the-art attention.

Less severe TBI can be missed, particularly in patients with multiple and life-threatening injuries who may be in shock, undergoing emergency surgery, sedated, or on a ventilator. When they are stabilized, their management will depend somewhat on the service to which they are transferred and on its awareness of the possibility of concurrent injuries.

Identification of TBI in electronic medical records of patients with SCI in this study was inconsistent. It might be thought that this was because the head injury was mild in this series of patients, but 55 percent of the Veterans with concurrent TBI and SCI were identified as having cognitive impairment. This is similar to the percentage found in patients with SCI treated in the SCI model systems of care. While cognitive impairment can be due to causes other than TBI in these patients, it remains important to identify whether they have had a TBI. During annual evaluations of Veterans with SCI, our VA SCI service psychologists evaluate attention, problem solving, processing speed, and memory by interview, and if cognitive impairment is suspected they supplement the interview with neuropsychological tests selected on the basis of the impairment suspected. The most frequent terms used in the electronic medical record for cognitive impairment were slowed processing speed and "short-term memory loss," although it is now recognized that it would be beneficial to use clearer terms to describe attention and memory in the medical record. In the past, the term short-term memory loss used in the medical record has often been nonspecific and may have been used to refer to anything from working memory of a few seconds to recall of the events from a few weeks before.

In the case of patients with mild TBI, it might have been argued in the past that they did not suffer greatly from delayed or absent documentation of the injury, but there is now increased interest in the unknown long-term effects of mild and repeated TBI on conditions such as Parkinson disease and dementia. The fact that the VA healthcare system follows patients with SCI for life offers an opportunity to study the relationship between these conditions.

The use of an electronic medical record in the VA has had many advantages, but it may be necessary to structure the collection and recording of some information in a more consistent way that could be implemented in a national system of care. Consistent screening of patients with SCI for TBI during their initial rehabilitation should be done to avoid missing the diagnosis of TBI. If TBI resolves, there is no way to identify it subsequently other than history from the patient, collaterals, and prior medical reports. Screening will need to be done after patients are stabilized on medications for pain and spasticity since these medications are known to affect cognitive functioning until patients accommodate to them. Patients will also need to be clear of delirium from surgical anesthesia, urinary tract infections, and other SCI complications. In many cases, it will be difficult to distinguish TBI from depression, posttraumatic stress disorder, and/or anxiety, so diagnosis will be delayed until psychiatric symptoms are adequately treated. These are some of many reasons for providing adequate time for rehabilitation rather than discharging patients as soon as they can survive outside of a hospital. Fortunately, adequate admission time is standard practice in the VA. It is possible that our finding that 50 percent of Veterans who experienced traumatic SCI in the last 10 yr are currently being recorded as having a concurrent TBI is still an underestimate, so there may still be a significant number of Veterans in whom TBI has not been diagnosed as suggested by the recent study in civilians [4]. It is critically important to avoid missing the diagnosis of TBI in Veterans (and others) if appropriate rehabilitation and follow-up care is to be provided.

The causes of SCI in Veterans with concurrent TBI, such as motor vehicle accidents, falls, and sporting accidents, resemble the causes seen in the civilian population, so some of the conclusions of this study may be applied to civilians. It would be of value to improve documentation of TBI in the civilian population with SCI, particularly as electronic medical records are being adopted. This could best be done within the SCI model systems, even though only a minority of U.S. civilians with SCI receives their care in these systems and they may have a higher proportion of patients with severe SCI than in the population treated outside the SCI model systems. Such documentation would allow for the collection of data in civilians comparable to that in Veterans and provide guidelines for future management of long-term consequences of these injuries, especially in young people.

CONCLUSIONS

1. Documentation of TBI in this population of Veterans with traumatic SCI was inconsistent; in patients with both SCI and TBI, the TBI identified by searching the notes in the electronic medical record was only recorded in the Active Problems list 18 percent of the time and was often absent from admission histories and discharge summaries.
2. Recorded incidents of TBI in Veterans with traumatic SCI in this study have increased from <9 percent before 1983 to 50 percent since 2003. This may reflect improved documentation and increased awareness, but there may be more cases that are still not being identified. Extrapolation of these figures nationally suggests that there may be a substantial number of Veterans whose TBI has not been documented.
3. Improved screening and documentation would help to identify all Veterans with both SCI and TBI and allow appropriate management and long-term follow-up.
4. Based on these findings, we propose the following recommendations:
 - a. Screening by a psychologist of all Veterans newly enrolled in the VA System of Care for Spinal Cord Injuries and Disorders to assess for potential TBI, because all VA SCI centers are required to have a psychologist in their team.
 - b. Structuring documentation of TBI in the CPRS at least in the Active or Inactive Problems lists and perhaps in other locations and templates.
 - c. Making available the baseline automated neuropsychological assessment data now collected on all U.S. military personnel to VA clinicians in the VA CPRS and using these data to assist in screening all patients with SCI for TBI when they are enrolled in the VA System of Care for Spinal Cord Injuries and Disorders.
 - d. Training of medical residents, fellows, and other physicians who work with SCI to screen for TBI.
 - e. Screening for TBI in non-Veteran populations with traumatic SCI, with documentation led by the SCI model systems and their database in the National Spinal Cord Injuries Statistical Center.

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Analysis and interpretation of data: G. H. Creasey, Z. C. Lateva, J. Rose, S. M. Schüssler-Fiorenza Rose.

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Mean Arterial Blood Pressure Correlates with Neurological Recovery after Human Spinal Cord Injury: Analysis of High Frequency Physiologic Data

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Abstract

Current guidelines for the care of patients with acute spinal cord injuries (SCIs) recommend maintaining mean arterial pressure (MAP) values of 85–90 mm Hg for 7 days after an acute SCI however, little evidence supports this recommendation. We sought to better inform the relationship between MAP values and neurological recovery. A computer system automatically collected and stored q1 min physiological data from intensive care unit monitors on patients with SCI over a 6-year period. Data for 100 patients with acute SCI were collected. 74 of these patients had American Spinal Injury Association Impairment Scale (AIS) grades determined by physical examination on admission and at time of hospital discharge. Average MAP values as well as the proportion of MAP values below thresholds were explored for values from 120 mm Hg to 40 mm Hg in 1 mm Hg increments; the relationship between these measures and outcome was explored at various time points up to 30 days from the time of injury. A total of 994,875 q1 min arterial line blood pressure measurements were recorded for the included patients amid 1,688,194 min of recorded intensive care observations. A large proportion of measures were below 85 mm Hg despite generally acceptable average MAP values. Higher average MAP values correlated with improved recovery in the first 2–3 days after SCI while the proportion of MAP values below the accepted threshold of 85 mm Hg seemed a stronger correlate, decreasing in strength over the first 5–7 days after injury. This study provides strong evidence supporting a correlation between MAP values and neurological recovery. It does not, however, provide evidence of a causal relationship. Duration of hypotension may be more important than average MAP. It provides support for the notion of MAP thresholds in SCI recovery, and the highest MAP values correlated with the greatest degree of neurological recovery. The results are concordant with current guidelines in suggesting that MAP thresholds >85 mm Hg may be appropriate after acute SCI.

Key words: blood pressure; mean arterial pressure; neurocritical care; neuroprotection; outcome; recovery; secondary injury; spinal cord injury

Introduction

SPINAL CORD INJURY (SCI) leaves patients with often profound deficits of motor, sensory, sexual, and sphincter function. In recent decades, we have learned much about molecular secondary injury processes that cause progressive, delayed damage to the injured spinal cord^{1–3}; however, we remain without a safe and efficacious therapeutic agent that targets them.^{4,5} We have also learned much of secondary insults such as hypoxia and hypotension that occur at the level of the organism and serve to exacerbate the injury to the spinal cord.^{6–9} Attention to preventing or aggressively treating secondary insults is currently the mainstay of care that follows SCI.^{10–13}

In 2002, the first guidelines for the management of acute SCI were published.¹² These guidelines recommended at the option level that hypotension—defined as a systolic blood pressure <90 mm Hg—should be avoided and that a mean arterial blood pressure (MAP) of 85–90 mm Hg should be targeted in the first 7 days after SCI. These recommendations were essentially unchanged in the 2013 update of the guidelines.¹³ A small, heterogeneous group of uncontrolled, underpowered studies supports this recommendation¹⁴; to date, no study provides better than class III evidence supporting blood pressure augmentation for acute SCI. In all relevant publications to date, blood pressure augmentation was merely part of an aggressive management protocol confounding the relationship between MAP and outcome.^{15–19} Moreover,

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comparisons have been made to historical controls in all cases. The current recommendations are largely based on the findings of a pilot study conducted by Vale and associates.¹⁷ The result is that hospitals devote substantial resources to monitoring and augmenting blood pressure in patients who may otherwise be suitable for treatment in less resource-intensive environments, despite only modest evidence supporting this practice.

Advances in computing now allow the continuous collection and storage of high frequency physiological data and the opportunity to study the impact of this physiology with substantially greater precision than was possible previously. Our group developed a system that collected and stored data once per minute for all patients monitored in the intensive care unit (ICU). This system automatically collected data for every patient with SCI admitted to San Francisco General Hospital (SFGH) over a 6-year period affording the opportunity to study the relationship between high-frequency physiological data and outcome. Although this correlative approach does not establish causation, it provides significant insights into this relationship.

Methods

Patient demographics and management

SFGH is the only Level 1 trauma center in San Francisco and the northern San Francisco peninsula. The hospital provides care for a high volume of patients with neurotrauma and polytrauma. Patients

with SCIs were admitted to the neurosurgical ICU, and a MAP of at least 85 mmHg was targeted for 5 days after the injury, similar to published guidelines¹² and the protocol of Wolf and colleagues.¹⁶ Pharmacological agents were administered if needed to achieve this goal.²⁰ In 26.8% of patients, the first pressor started was phenylephrine. In 48.5%, the first pressor used was dopamine. In 3.1%, dopamine and phenylephrine were started concurrently. In 1.0%, levophed was the first used vasopressor. In 23% of patients, a second vasopressor was needed to meet the MAP targets. A detailed study of vasopressor use in an overlapping subset of SCI patients from San Francisco General Hospital has been published recently.²⁰

Patients were identified retrospectively for this analysis. Demographic data were collected from the patients' health records as shown in Table 1. American Spinal Injury Association Impairment Scale (AIS) grades were computed based on detailed neurological examinations performed on presentation but after resuscitation, and just before discharge.²¹ The AIS grade improvement was calculated. Because of the limited neurological recovery known to occur in patients with AIS grade A injuries post-resuscitation, analyses were planned with and without these patients included *a priori*.

Data collection

Our institution developed a research ethics board approved computerized data acquisition system in conjunction with Aristain Bioinformatics LLC, which collects and stores data from the patients' bedside monitor in the neurosurgical ICU. The same system was used to collect physiological data in nonhuman experimentation as described previously by our group.²² Variables displayed on the

TABLE 1. CHARACTERISTICS OF STUDIED PATIENTS BASED ON DEGREE OF NEUROLOGICAL IMPROVEMENT

	No outcome data (n = 26)	No improvement (n = 35)	1 AIS point improvement (n = 23)	> 1 AIS point improvement (n = 13)	p value
Sex	43.0 ± 16.1 20 M, 6 F	42.5 ± 19.0 28 M, 7 F	50.2 ± 22.3 15 M, 8 F	52.2 ± 18.8 10 M, 3 F	0.434 0.639
ISS	27.6 ± 16.4	30.1 ± 14.7	25.4 ± 14.3	25.6 ± 9.7	0.622
AIS A	?	23 (65.7%)	3 (13.0%)	3 (23.1%)	< 0.0001
AIS B	?	1 (2.8%)	1 (4.3%)	3 (23.1%)	0.093
AIS C	?	3 (8.6%)	6 (26.1%)	4 (30.8%)	0.131
AIS D	?	5 (14.3)	11 (47.8%)	2 (15.4%)	0.016
AIS E	?	0 (0%)	2 (8.7%)	1 (7.7%)	0.995
Surgery	4 (15.4%)	33 (94.3%)	19 (82.6%)	13 (100%)	< 0.0001
Timing of surgery	24.0 h ± 32.5	36.4 h ± 32.5	42.9 h ± 75.8	42.0 h ± 35.5	0.917
Total hospital days	47.3 ± 48.1	26.8 ± 37.0	17.9 ± 13.9	56.2 ± 49.9	0.074
Total measurements	17421.3 ± 27133.5	15671.1 ± 14970.9	12946.4 ± 14874.4	21958.5 ± 22254.0	0.200
Penetrating	0 (0%)	8 (22.8%)	2 (8.7%)	0 (0%)	0.006
Cervical	1 (20%)	18 (54.5%)	16 (72.7%)	12 (92.3%)	0.080
Thoracic	0 (0%)	13 (39.3%)	3 (13.6%)	1 (7.7%)	0.171
Lumbar	4 (80%)	1 (3.0%)	2 (9.1%)	0 (0%)	0.024
Required two vasopressors	1 (20%)	11 (31.4%)	5 (21.7%)	3 (23.1%)	0.927

AIS, ASIA Impairment Scale¹⁻³; here, AIS A-E denote the post-resuscitation score; ISS= Injury Severity Score.⁴

Characteristics of analyzed patients are shown with grouping based on change in neurological function by time of discharge. For continuous data means are presented ± standard deviation. For categorical data, frequencies are presented as well as percentage of patients for whom data were available. Three patients who exhibited neurological worsening were excluded because of small sample size (n=3). The p values reflect the results of univariate statistical analysis. Analysis of variance was performed for continuous data, and binomial logistic regression was used for categorical variables. Statistically significant values are italicized.

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4. Baker, S.P., O'Neill, B., Haddon, W., Jr., and Long, W.B. (1974). The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J. Trauma* 14, 187-196.

bedside monitor were collected at 1 minute intervals, and for this work, MAP values as measured with an arterial line were analyzed. The duration of arterial line blood pressure monitoring was based solely on medical necessity as judged by the treating intensivist.

Data were recorded continuously and automatically from every bedside monitor in the neurosurgical ICU between 2005 and 2011 and stored on a server in a fashion adherent to patient privacy regulations. Data acquisition with this system initiates automatically as soon as patient data appear on the bedside monitor. The time of the first recorded observation in the collection system was denoted as time “1”. Note that this is distinct from the time of injury or the first arterial line MAP measurement.

Data analysis

MAP values were analyzed with the assistance of Matlab. We designed a program to extract MAP values for each patient stored in individual Excel files. It calculated average MAP values between periods specified by the analyst. It was also programmed to count the number of epochs with MAP values below specified thresholds between specified periods. We selected to analyze blood pressures below 80 different thresholds from 120 to 40 mm Hg (1 mmHg increments). The Matlab program was checked for errors by comparing results with those generated using Microsoft Excel. The proportion of values below thresholds was analyzed to account for different numbers of observations between patients. Microsoft Excel and PowerPoint were used to graph the data and Photoshop CS2 was used to combine images for figures. Error bars represent standard error of the mean in all cases.

Statistical analysis

SPSS v21 software was used for statistical analyses. Analysis of variance was used as a first step in the analysis of average values from continuous data; if a difference between groups was demonstrated, the Tukey and Bonferroni *post hoc* tests were performed that adjust for multiple comparisons. Binomial logistic regression was used to analyze dichotomous categorical data. For average values of continuous data, the “n” was considered to be the total number of observations. Where proportions were analyzed, a single proportion was calculated for each patient, and the “n” was thus the number of patients in each group.

Results

Characteristics of included patients

One hundred patients with SCI were identified with continuous physiological data recordings. These patients had a total of 1,688,194 minutes of recorded observation corresponding to 1172.4 days of total observation. A total of 994,875 q1 min MAP measurements were recorded corresponding to 690.1 days of MAP observations. We restricted our analysis to those values recorded in the first 30 days of hospitalization.

Of the 100 patients, it was possible to calculate the change in AIS grade between post-resuscitation and pre-discharge values for 74. Of these, three patients experienced neurological worsening, 35 exhibited no change in AIS grade, 23 had improved one AIS grade, and 13 improved more than one AIS grade. There were 27 patients who had AIS grade A injuries; when removed from the dataset, 2 patients experienced neurological worsening, 12 exhibited no change in AIS grade, 21 improved one AIS grade, and 10 exhibited more than 1 grade of improvement. The neurological improvement seen in our study was comparable with other recent publications.^{23,24} We excluded patients with neurological worsening from subgroup analyses given that robust conclusions could not be generated and the fact that the two patients who remained

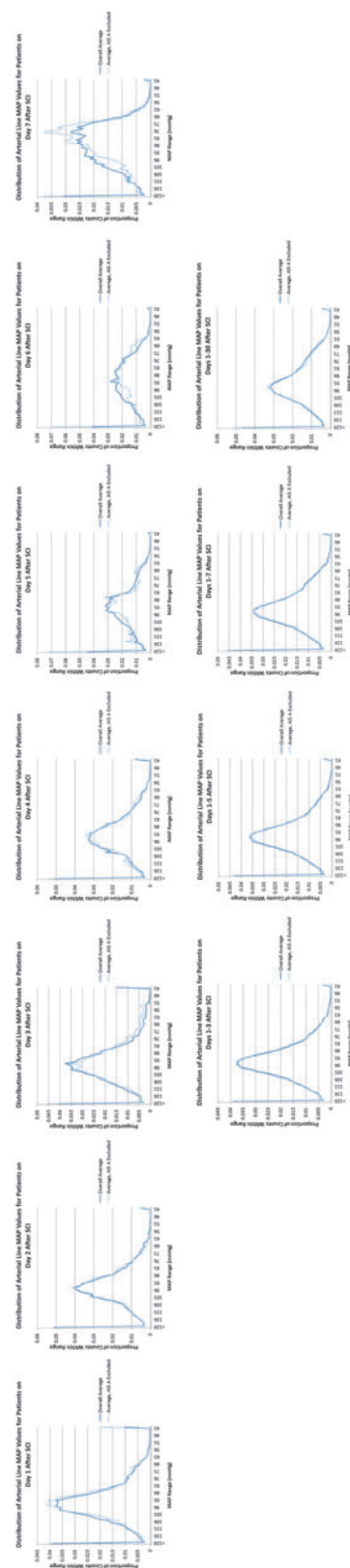


FIG 1. Distribution of mean arterial pressure values demonstrates a high proportion of measurements were below treatment threshold. The proportion of mean arterial pressures (MAPs) within 1 mm Hg ranges are plotted. Values were measured with an arterial line. The solid line includes all patients ($n = 100$), while the dashed line excludes patients who were American Spinal Injury Association Impairment Scale (AIS) grade A on final neurological assessment ($n = 73$). Here the indicated time is in reference to the time of intensive care unit admission. SCI, spinal cord injury. Color image is available online at www.liebertpub.com/neu

could not be included in statistical analyses when AIS grade A patients were excluded.

Patient demographics

Characteristics of studied patients are recorded in Table 1. Patients with penetrating SCI were significantly less likely to improve neurologically ($p=0.006$, binomial logistic regression). Patients with lumbar injuries were significantly less likely to have outcome data collected for analysis ($p=0.024$, binomial logistic regression). Although not significant, patients achieving >1 AIS grade improvement had substantially longer periods of observation in the ICU and a longer period of hospitalization potentially providing greater opportunity for neurological improvement than in other groups. Although the degree of neurological improvement is

positively correlated with length of stay, the R^2 value is only 0.0484, indicating that the strength of this confound is quite weak (Supplementary Fig. 1; see online supplementary material at ftp.liebertpub.com).

Of note, 100% of patients with outcome data available needed pressor administration to achieve MAP goals. An approximately equal number of patients in each group needed a second vasopressor for blood pressure augmentation. Significantly fewer patients with missing outcome data were documented as having undergone surgery. Of those patients initially AIS grade A, a significantly greater proportion of patients exhibited no neurological improvement than some improvement. Of those patients initially AIS grade D, a significantly greater proportion of patients exhibited a single grade of neurological improvement than no improvement.

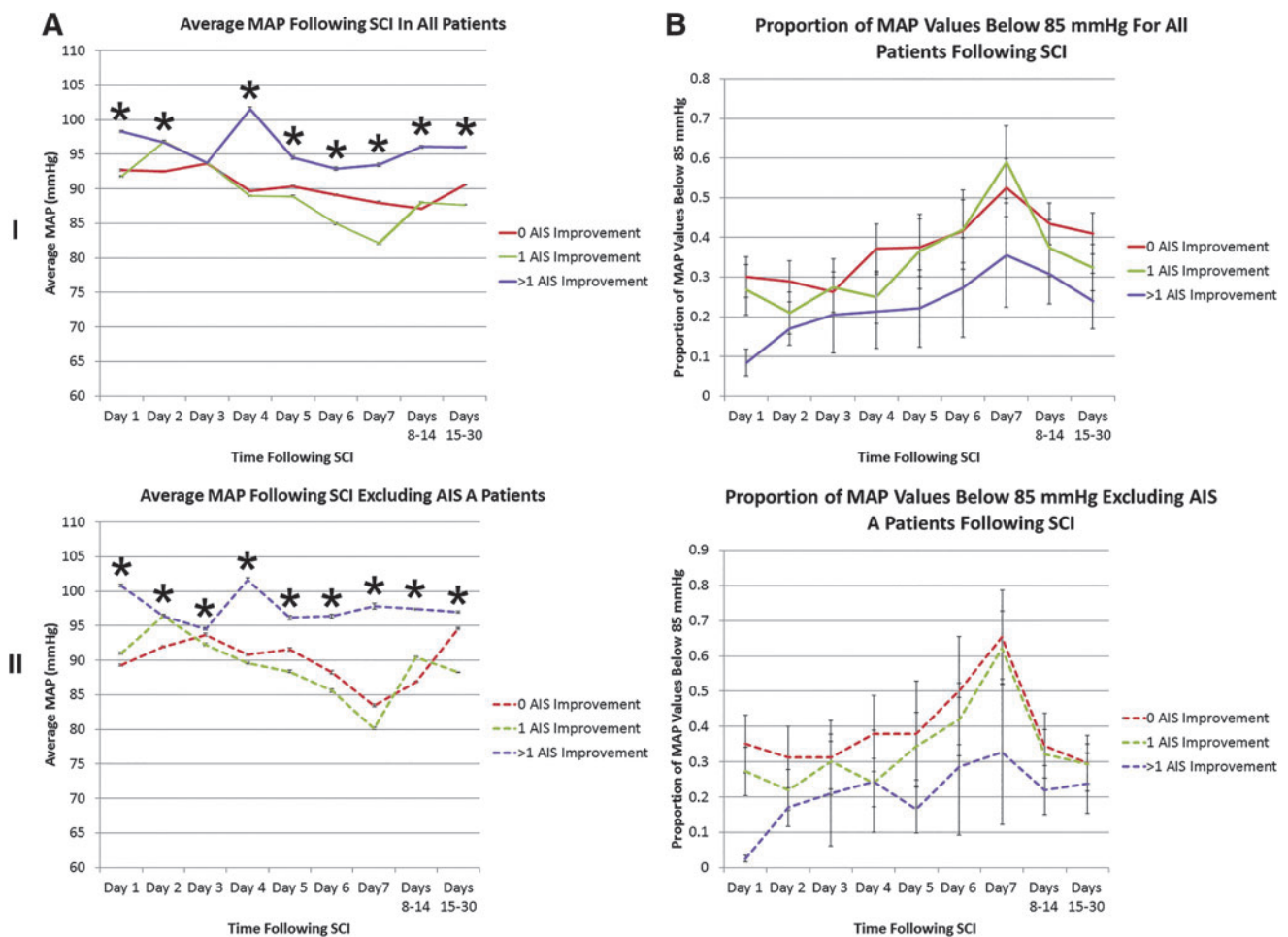


FIG. 2. Average mean arterial pressure (MAP) and proportion of values <85 mm Hg are associated with outcome early after spinal cord injury in a noncumulative analysis. In (A), average MAP values are plotted in relation to time subsequent to intensive care unit admission. Values were measured with an arterial line. In (B), the proportion of MAP values below the lower limit of the recommended blood pressure range (85 mm Hg) are plotted. In (I), all patients with outcome data are plotted, while in (II), patients known to be American Spinal Injury Association Impairment Scale (AIS) grade A at final neurological examination are excluded. The latter case is denoted with dashed lines. For (A), the “n” used in statistical testing was the number of blood pressure measures, while in (B), it was the number of patients.

SCI, spinal cord injury.

*Denotes significance on analysis of variance performed at each time point. Error bars represent standard error.

I: For the group with 0 AIS grade improvement, $n=35$ patients; the group with 1 AIS grade improvement, $n=23$ patients, and the group with >1 AIS grade improvement, $n=13$ patients.

II: For the group with 0 AIS grade improvement, $n=13$ patients; the group with 1 AIS grade improvement, $n=21$ patients, and the group with >1 AIS grade improvement, $n=10$ patients. Color image is available online at www.liebertpub.com/neu

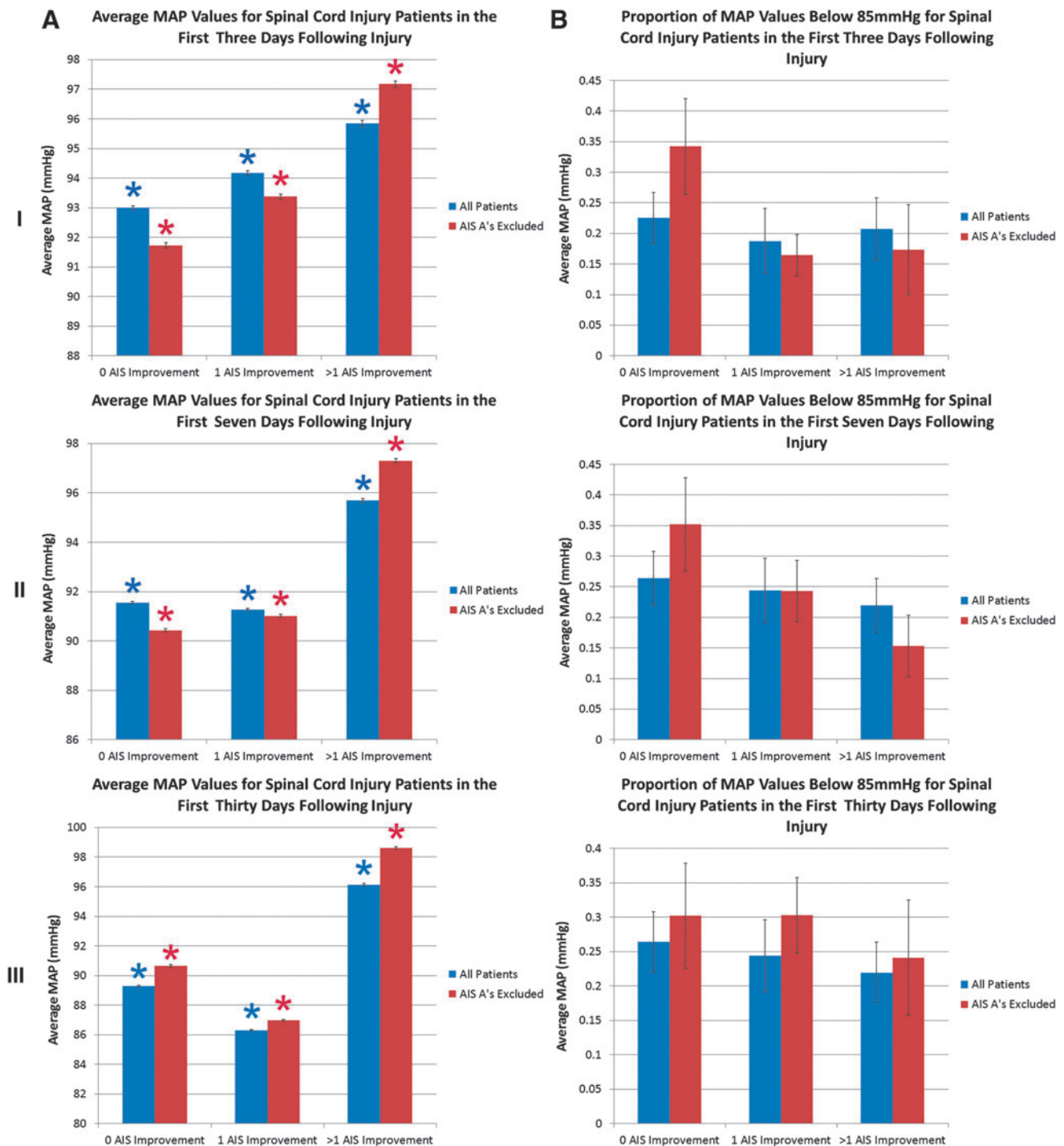


FIG. 3. Average mean arterial pressure (MAP) and proportion of values <85 mm Hg are significantly associated with outcome early after spinal cord injury in a cumulative analysis. In (A), average MAP values are plotted. In (B), the proportion of MAP values below the lower limit of the recommended blood pressure range (85 mm Hg) are plotted. Values were obtained from arterial line measures, and times reflect the interval since intensive care unit admission. In (I), values for days 1–3 post-spinal cord injury are presented. In (II), values for days 1–7 post-spinal cord injury are presented. In (III), values for days 1–30 post spinal cord injury are presented. For data including all patients (blue), the group with 0 AIS grade improvement, $n = 35$ patients; the group with 1 AIS grade improvement, $n = 23$ patients; and the group with >1 AIS grade improvement, $n = 13$ patients. For data excluding patients AIS grade A on their final neurological examination (red), the group with 0 AIS grade improvement, $n = 13$ patients; the group with 1 AIS grade improvement, $n = 21$ patients, and the group with >1 AIS grade improvement, $n = 10$ patients.

*Denotes a statistical difference from all other groups on *post-hoc* Bonferroni testing subsequent to a significant overall analysis of variance. Error bars represent standard error. For (A), the “n” used in statistical testing was the number of blood pressure measures, while in (B), it was the number of patients. Color image is available online at www.liebertpub.com/neu

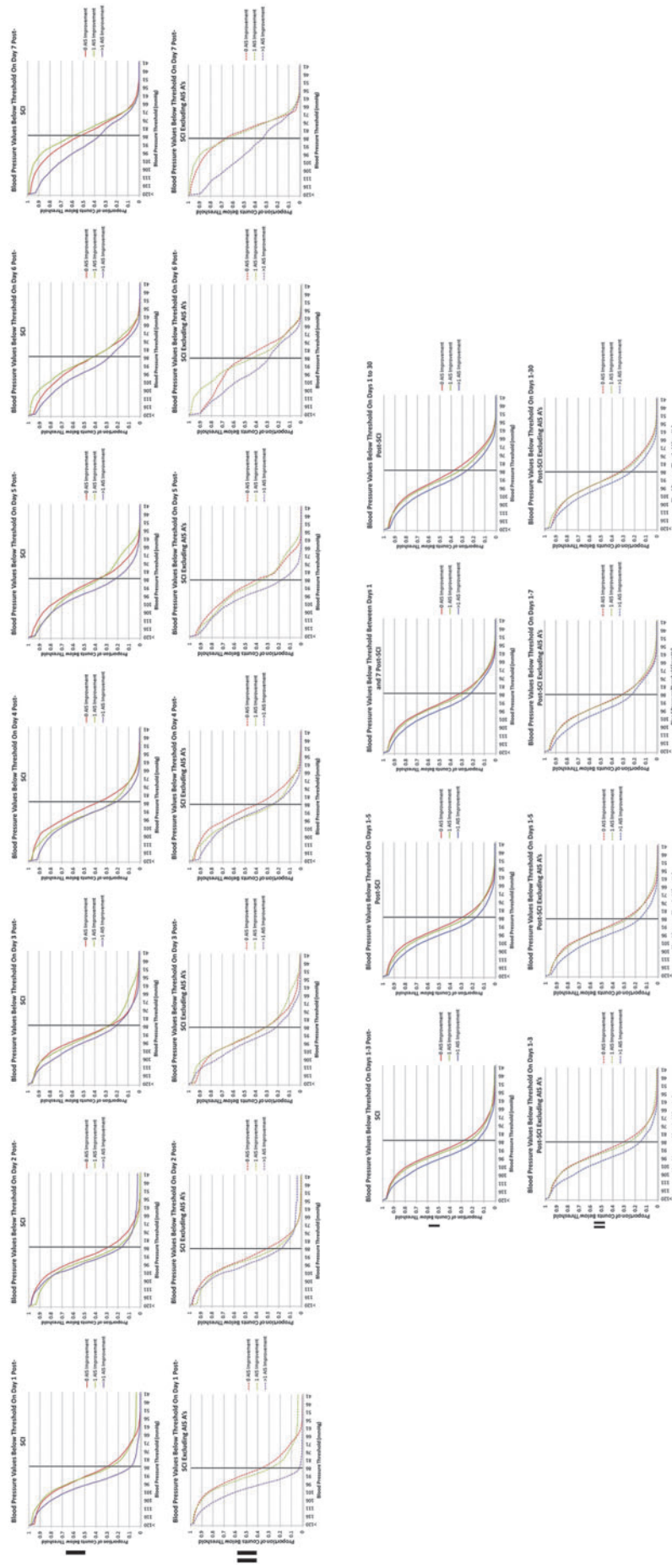


FIG. 4. Duration of hypotension early after injury is related to poorer neurological recovery. Plots of the proportion of mean arterial pressure (MAP) values below thresholds are shown for patients in 1 mm Hg increments. In **(I)**, all patients with outcome data are plotted, while in **(II)**, patients who were AIS grade A on final neurological assessment were excluded (as denoted by the dashed lines). Values were measured with an arterial line, and times reflect the interval since intensive care unit admission. The black vertical lines denote 85 mmHg, the lower end of the currently accepted target for blood pressure in the first 7 days after spinal cord injury.

I: For the group with 0 AIS grade improvement, $n = 35$ patients and 336,601 measurements at 30 days. For the group with >1 AIS grade improvement, $n = 23$ patients and 183,541 measurements at 30 days. For the group with >1 AIS grade improvement, $n = 13$ patients and 136,278 measurements at 30 days.

II: For the group with 0 AIS grade improvement, $n = 13$ patients and 116,165 measurements at 30 days. For the group with 1 AIS grade improvement, $n = 21$ patients and 149,565 measurements at 30 days. For the group with >1 AIS grade improvement, $n = 10$ patients and 67,259 measurements at 30 days. Color image is available online at www.liebertpub.com/neu

Distribution of MAP for all patients after SCI

The distribution of MAP values for all 100 patients at various time points subsequent to SCI is demonstrated in Figure 1. Figure 1 presents a frequency plot of the proportion of counts in 1 mm Hg blood pressure ranges between 40 and 120 mm Hg. Plots are also shown with the exclusion of patients who were AIS grade A on final neurological examination (dashed lines). While most measured MAP values were above the 85 mm Hg treatment threshold, 42.1% of all recorded MAP values within 30 days of injury were below 85 mm Hg. In the first 7 days, 28.8% of measures were below the recommended treatment threshold of 85 mm Hg. During the first 5 days, while an attempt was made to meet the MAP target, 24.9% of measures were below the 85 mm Hg threshold. Exclusion of AIS grade A patients did not substantially alter the distribution of measures. Of note, the curves generally conform to a bell-shape with minimal skew; values above the mean were generally as probable as those below without apparent influence of the 85 mm Hg threshold.

Relationship between average MAP, time below MAP threshold, time from ICU admission and neurological improvement

In Figure 2, average MAP values and the proportion of MAP values below 85 mm Hg are plotted for groups segregated by amount of neurological improvement for various noncumulative time points subsequent to ICU admission. Average MAP values were uniformly >85 mm Hg during the 5 days that MAP targeting was used. Despite this, a large proportion of MAP measurements were below this threshold at every examined time point. Average MAP values are thus insensitive to episodes of hypotension or time below treatment threshold.

The group achieving >1 AIS grade improvement had the highest MAP and lowest proportion of measures below 85 mm Hg at every examined time point whether or not AIS grade A patients were included in the analysis. MAP was higher in the group achieving 1 AIS grade improvement than in the group that did not improve only for the first 24–72 h after ICU admission. Patients achieving 1 AIS grade improvement had a lower proportion of MAP measures below 85 mm Hg than in the group that did not improve only for the first 5–7 days after ICU admission. This difference seemed to lessen with time, however.

A cumulative analysis of values in the first 3, 7, and 30 days is presented in Figure 3. A higher average MAP correlated with outcome in the first 3 days after injury; however, by 7 days, higher MAP values were only noted in the group achieving >1 AIS grade improvement. The proportion of measures <85 mm Hg was generally associated with outcome at all time points after injury. As in Figure 2, results were similar whether or not AIS grade A patients were included or excluded from the analysis.

MAP thresholds and neurological improvement after SCI

To explore the notion of MAP thresholds, we plotted the proportion of values below 80 different and physiologically relevant MAP thresholds for groups based on degree of neurological improvement (Fig. 4). When lines cross, diverge, or are separated, an effect of MAP on outcome is possible. The group achieving >1 grade of AIS grade improvement had a reduced number of measures below all examined MAP thresholds compared with groups with less improvement—and this difference was particularly marked in the first 24 h. The lowest MAP at which patients with no

improvement were distinguished from those with 1 grade of improvement was 70–75 mm Hg, suggesting that this may be the lowest blood pressure threshold associated with neurological benefit. Moreover, these two lines tended to re-converge around 95 mm Hg, suggesting that values above this level are not related to the one grade of neurological improvement discerning these groups. The gap between plotted lines for the group that did not improve and that which improved one grade decreases over time, providing additional evidence that the neuroprotective effect of MAP elevation decreases with time from injury. A threshold discriminating patients with >1 AIS grade improvement from other groups is not suggested.

Discussion

Spinal cord ischemia is believed to play a central role in the secondary injury processes that cause delayed and progressive injury to the spinal cord after the initial—or primary—SCI has ceased.^{1,2} This secondary injury can be exacerbated by secondary insults such as hypotension and hypoxia, which are, unfortunately, common in patients with SCIs who frequently exhibit neurogenic and/or hemorrhagic shock.^{8,9,18,25,26} Spinal cord blood flow has been subject to detailed study in animal models of SCI, and its impairment is believed to contribute to neurological injury after SCI.^{27–29} Moreover, patients with SCI frequently exhibit autonomic and hemodynamic instability in the first week after injury.^{30,31}

There is thus a strong rationale for ICU monitoring and blood pressure support early after SCI. Conceptually, we can think of blood pressure support as achieving a higher than normal pressure to augment the delivery of nutrients to injured tissue or as preventing hypotension and a deficiency of nutrient supply.¹⁸ These two notions of blood pressure support should be considered separately and are worthy of independent study.

Hospitals caring for patients with SCI spend millions of dollars each year to comply with the published guidelines despite the very weak supportive data⁹ and known complications that can occur as a result of vasopressor administration^{20,32} or the bed rest with which it is associated.^{33–35} Our institution estimates that the cost of ICU care is \$2500–\$4000 a day. It is estimated that there are 12,500 SCIs in the United States annually.³⁶ The cost of 7 days of ICU care for these patients is thus estimated to be \$218,750,000–\$350,000,000 with the cost of each day of monitoring costing \$31,250,000–\$50,000,000. Indeed, in this study all patients for whom outcome data were available needed vasopressor therapy to achieve the target MAP, and this is consistent with other published reports¹⁷; the need to administer vasopressors is largely implicit with following the guidelines. Given this, the notion of blood pressure augmentation as a neuroprotective strategy after acute SCI needs further study as a high priority.

The present study is unique in that it has been able to correlate high-frequency blood pressure measures from a large cohort of patients with SCI with outcome. Although it cannot provide evidence for causation, it does provide important information about the relationship. Notably, the findings of this study were robust and generally consistent irrespective of the time frame analyzed and whether or not AIS grade A patients were included. It is critical to note that a correlation between blood pressure and severity of SCI has been previously reported and is an important potential confound.^{19,30} Nonetheless, this study is noteworthy for suggesting that both MAP augmentation and the avoidance of hypotension could have neuroprotective effects, and it informs the time frame over which these effects may be relevant.

Literature to date

A small number of studies provide class III evidence for observing patients in the ICU for 7 days after SCI and maintaining a target MAP >85 mm Hg.^{9,12,13} In 1976, Zach and associates¹⁵ published a prospective study of 117 patients with SCI that reported a high level of conversion from complete to incomplete injuries when early aggressive treatment was undertaken; however, this study did not use a control group and did not specifically study nor report on the issue of MAP augmentation. In 1977 Hachen et al. reported a series of 188 patients who were rapidly admitted to intensive care and exhibited a much better mortality rate compared with statistics from 1966.³⁷ In 1979, Gschaedler and co-workers³⁸ reported a similar study involving 51 patients and similar findings.

In 1984, Tator and colleagues¹⁸ published a series of 144 patients whom they compared with historic controls. These patients were treated with aggressive efforts to avoid hypotension and hypoxia, and they received this care more rapidly than the control group. The more aggressive management protocol was associated with lower mortality, morbidity, and healthcare costs. In 1991, Wolf and associates¹⁶ studied 52 patients with bilateral cervical facet dislocations for whom they targeted a MAP >85 mm Hg for 5 days amid a paradigm emphasizing rapid medical and surgical treatment. The authors claimed neurological improvement; however, no comparison with controls was made. In 1993, Levi and coworkers¹⁹ instead targeted a MAP >90 mm Hg as part of their aggressive SCI management paradigm. In their report of 50 patients, they concluded that aggressive care reduced mortality and morbidity; however, it did not include a control group.

Vale and associates¹⁷ reported a “pilot study” of 77 patients who underwent aggressive volume expansion with Swan-Ganz catheter monitoring, and a target of MAP >85 mm Hg for 7 days after injury. The authors concluded that the better-than-expected outcomes seemed attributable to their emphasis on hemodynamic parameters; however, no comparison was made with a control group, and the 7-day period was picked arbitrarily. This study largely serves as the basis for the current guidelines for the acute cardiovascular management of patients with SCIs.^{12,13}

Cohn and coworkers¹⁴ more recently reported a retrospective study of the relationship between episodes of hypotension noted in the medical record and outcomes using step-wise regression, and concluded that there may be a threshold of around 70 mm Hg below which worse outcomes are seen. This study involved only 17 patients and had less accurate data on brief periods of hypotension, but its results are in accordance with our findings (Fig. 4).

Few strong conclusions can be drawn from the literature to date. A major limitation of these studies is a lack of evidence about patients’ actual blood pressures—simply allocating a patient to a blood pressure target does not mean that the patients achieved it nor does it exclude substantial periods of hypotension. This is evidenced in our own work by the fact that nearly a third of the recorded values for our patients were below treatment threshold despite efforts to prevent this (Fig. 1, 2, 4).

Another important limitation of publications to date is that blood pressure augmentation was co-administered with other aggressive management strategies, preventing a causal relationship from being established. As well, no study made a comparison to appropriate contemporaneous controls—where a comparison was made it was to historical or previously published controls. Lastly, the distinct issues of avoiding values below threshold and elevating MAP above threshold were insufficiently distinguished by these studies.

A suggestion of time frames, thresholds, and the importance of avoiding MAPs below treatment threshold

Our study found that average MAP values correlated with outcome for only 2–3 days after ICU admission, which is noteworthy given that current guidelines recommend targeting a MAP >85 mm Hg for 7 days after injury. The proportion of values below threshold correlated with outcome for 5–7 days after injury, although the magnitude of this relationship decreased over time (Fig. 2, 3). Indeed, the group achieving >1 AIS grade of improvement had a substantially lower burden of hypotension than other groups in the first 24 h compared with other time points (Fig. 4). Taken together, these data suggest that the duration of time below treatment threshold may have a more important influence on neurological outcome than the average MAP,¹⁸ and it provides support for the notion of blood pressure monitoring and augmentation for 5–7 days after SCI.

MAP thresholds are suggested when the plotted lines in Figure 4 diverge or cross. The gap between plotted lines for the group exhibiting no improvement and that which improved 1 AIS grade was a robust finding in our work. The divergence was generally noted around 70–75 mm Hg, and the lines tended to converge again around 90–95 mm Hg. The three groups are most robustly discriminated by a MAP around 85 mm Hg, providing support for the treatment threshold recommended in the acute SCI guidelines.^{12,13}

Our study suggests that neurological benefit may begin around MAP values of 70–75 mm Hg, consistent with the report of Cohn and coworkers.¹⁴ A threshold associated with the achievement of >1 grade of AIS improvement was not clearly evident. Given the consistent suggestion of higher MAP values and less hypotension in this group, we cannot exclude the possibility that a higher MAP target may contribute to greater degrees of neurological recovery.

Values below treatment threshold were frequent and yet not apparent in analysis of average MAP

The results shown in Fig. 1–4 are remarkable in demonstrating that a large proportion of measurements in our cohort of patients were below the treatment threshold despite an attempt to maintain MAP above the treatment threshold. Moreover, these values below threshold occurred despite consistent achievement of average MAP values above the threshold. Additionally remarkable is that at most time points, the distribution of MAP values approximated a normal distribution with values below the mean as likely as those above. Fewer values below the mean would have been anticipated. This speaks to the difficulty inherent to consistently achieving a MAP >85 mm Hg in patients with SCI who may have neurogenic and/or hemorrhagic shock and perhaps difficulty overcoming homeostatic mechanisms.

The suggested importance of relative hypotension has important implications for trial design. If a trial randomized patients to one MAP goal or another, high frequency MAP data would be important to ensure that the targets were actually reached for a significant duration of patient care. Moreover, it would play an important role in ensuring that hypotensive episodes do not confound putative effects of the target MAPs.

The clinical relevance of benefit that decreases over time

The finding that the benefit of MAP augmentation appears to decrease over time is of great clinical significance. Vasopressor

administration can be associated with complications such as cardiac dysrhythmia and cardiac ischemia.²⁰ The prolonged bed rest associated with MAP targeting accentuates SCI patients' already high risk of deep venous thrombosis and may be associated with an elevated risk of pressure sores, nosocomial infections, and deconditioning.^{33–35,39–41} In patients who show these or other adverse effects early in their course of care, a decreased length of administration may be appropriate, given that the risks of blood pressure augmentation²⁰ likely increase over time while the benefits seem to decrease. Moreover, these data suggest that it may be appropriate to aggressively treat patients for the first 1–2 days even if their deficits are mild or if they are presumed to be high risk for complications.

It is interesting to consider that there may also be increased benefit inherent to blood pressure augmentation at the earliest possible time after injury—in the emergency department or even by first responders, although defining the etiology of hypotension is critical before initiating pressors because mortality increases in hemorrhagic shock treated with pressors.⁴²

MAP augmentation might have a causal role in neurological recovery

As interesting observation in this study is the fact that after cessation of MAP augmentation after the fifth day of ICU care, the group achieving a single grade of AIS improvement had a higher proportion of MAP values below threshold than the group that did not improve, while previously the converse was true (Fig. 2). This suggests that the baseline blood pressure in the group exhibiting 1 grade of improvement was inherently lower and that the vasopressor therapy in this group led to higher values early after SCI. This does not prove that MAP augmentation caused the neurological recovery, but it does suggest this could be the case. Indeed, all patients with outcome data needed vasopressor therapy to achieve their MAP targets, and approximately the same number of patients in each group needed two agents, suggesting a similar burden of baseline hypotension. Moreover, the observed relationships were consistent whether or not AIS grade A patients were included in the analyses.

Despite the limited evidence supporting MAP augmentation after SCI, future trials that could establish a causal relationship will likely need to compare the current MAP target to one that is higher because a control group involving a lower target or no target would likely be judged unethical.

Limitations

In interpreting this study, a number of caveats are important to consider. Although the physiological data were collected prospectively, the remainder of this study was performed retrospectively. We did not have sufficient long-term follow-up data to use outcomes after discharge in our analysis. We were unable to calculate an AIS grade change for nearly a quarter of the patients in our study, which reflects challenges inherent to merging multiple medical record numbers for each patient at our institution and limited availability of research personnel.

The denoted time periods begin with the onset of ICU monitoring and not time from injury; this is, however, clinically relevant. As well, we do not have a record of the time at which blood pressure augmentation was initiated nor the patients' baseline blood pressure measures. Because MAP augmentation was ceased at 5 days, we are aware of the patients' blood pressure values after cessation of therapy, which provides similar information. Accordingly, the SFGH practice of maintaining MAP goals for 5 days after SCI

instead of 7 days must also be considered in the interpretation of these results.

There are a number of potential confounds in our study. A significant difference in the proportion of penetrating injuries among outcome groups is a potential confound; however, our findings were robust when patients with AIS grade A injuries at pre-discharge examination were excluded. The potential confounding effect of injury severity on MAP values has been noted.^{19,30} As discussed, all patients with outcome measures needed vasopressor therapy, and a similar proportion in each group needed two vasopressors to maintain MAP goals, which suggests a similar baseline burden of hypotension in each group and that differences in outcome could be related to the achieved MAP values. Also important is that the patients achieving >1 AIS grade of improvement stayed longer in the ICU and in the hospital on average and had greater opportunity for neurological improvement than the other groups. As discussed and illustrated in Supplemental Figure 1 (see online supplementary material at ftp.liebertpub.com), the confound associated with this effect appears to be minimal. As well, such a relationship was not evident for the group achieving 1 grade of improvement compared with the group that did not improve.

Conclusions

This is the first study to provide a detailed analysis of the relationship between high frequency MAP measures and extent of neurological improvement. Although this study cannot establish a causative relationship, it provides a wealth of information about the relationship. This study suggests that average MAP may only relate to neurological outcome in the first 2–3 days after injury. The duration of time below treatment threshold may be of greater relevance to neurological recovery—a relationship with outcome is suggested for 5–7 days after injury and the relationship seems to decrease in strength over time. These results are largely consistent with published guidelines for the management of acute SCI. Prospective study randomizing patients to different MAP targets will be an important next step for these patients.

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Author Disclosure Statement

No competing financial interests exist.

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Multidimensional Analysis of MRI Predicts Early Impairment in Thoracic and Thoracolumbar SCI

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Abstract

Literature examining MRI in acute spinal cord injury (SCI) has focused on cervical SCI. Reproducible systems have been developed for MRI-based grading, however it is unclear how they apply to thoracic SCI. Our hypothesis is that MRI measures will group as coherent multivariate principal component (PC) ensembles, and that distinct PCs and individual variables will show discriminant validity for predicting early impairment in thoracic SCI. We undertook a retrospective cohort study of 25 patients with acute thoracic SCI who underwent MRI upon admission and had American Spinal Injury Association Impairment Scale (AIS) at hospital discharge. Imaging variables of axial grade, sagittal grade, length of injury, thoracolumbar injury classification system (TLICS), maximum canal compromise (MCC), and maximum spinal cord compression (MSCC) were collected. We performed an analytical workflow to detect multivariate PC patterns followed by explicit hypothesis testing to predict AIS at discharge. All imaging variables loaded positively on PC1 (64.3% of variance), which was highly related to AIS at discharge. MCC, MSCC, and TLICS also loaded positively on PC2 (22.7% of variance) while variables concerning cord signal abnormality loaded negatively on PC2. PC2 was highly related to the patient undergoing surgical decompression. Variables of signal abnormality were all negatively correlated with AIS at discharge with the highest level of correlation for axial grade as assessed with the BASIC score. A multiple variable model identified BASIC as the only statistically significant predictor of AIS at discharge, signifying that BASIC best captured the variance in AIS within our study population. Our study provides evidence of convergent validity, construct

validity, and clinical predictive validity for the sampled MRI measures of SCI when applied in acute thoracic and thoracolumbar SCI.

KEY WORDS: MRI, spinal cord injury, thoracic, BASIC, T2 hyperintensity, TLICS

Introduction

Acute traumatic spinal cord injury (SCI) involving the thoracic and thoracolumbar spinal cord is considerably less common than cervical SCI with approximately 10% of SCI involving the thoracic spine and another 6% involving the cervicothoracic or thoracolumbar junctions.¹ Most of the literature examining MRI findings in acute traumatic SCI have focused on the more common injury to the cervical spinal cord with relatively little attention given to acute SCI caudal to the cervical level.²⁻²³ Anatomic and functional distinctions are significant between the cervical and more caudal spinal cord segments, suggesting imaging evaluation may in fact be level specific.^{24, 25}

Since the widespread adoption of MRI in evaluating the spinal cord in the acute setting, there have been numerous studies examining the prognostic value of MRI in acute cervical spinal cord trauma.^{2-5, 7, 9, 11-23, 26, 27} The majority of these studies have focused on the longitudinal extent of T2 signal abnormality in the sagittal plane or secondary markers of SCI such as canal and spinal cord compression in the cervical spine.^{2, 3, 5, 7, 9, 11-23, 26-29} However, the internal architecture of the spinal cord including the predominant longitudinal orientation of functionally important ascending and descending white matter tracts would suggest that the transverse extent of injury should be a strong predictor of clinical outcome;

this hypothesis has been corroborated by pre-clinical, and more recently, human studies.^{4, 8, 30-35}

A number of reproducible systems have been developed for MRI-based grading in acute SCI. The most recent addition is a grading system for the axial plane, termed the Brain and Spinal Injury Center (BASIC) score.⁴ The BASIC score can be used in combination with other measures including a commonly used sagittal grading system, the longitudinal extent of T2 signal abnormality, maximum canal compromise (MCC), maximum spinal cord compression (MSCC), and the thoracolumbar injury classification system (TLICS). With the exception of TLICS, these injury classification systems were initially developed for the more common cervical spinal cord injury but could have prognostic value throughout the spinal axis. In this study we aim to evaluate the application of the various MRI grading systems in the setting of acute thoracic SCI.

We applied multidimensional data-driven analytics to the full set of imaging classifications to assess validity of these MRI metrics for thoracic SCI. Our hypothesis is that the BASIC score and the other MRI measures of SCI will group together as coherent multivariate principal component (PC) ensembles, and that distinct PCs (PC1, PC2 etc.) will show discriminant validity for predicting distinct impairment patterns in thoracic and thoracolumbar SCI at time of patient discharge. To test this hypothesis, we performed an analytical workflow of data-driven-discovery to detect multivariate PC patterns followed by explicit hypothesis testing of whether the PCs and the individual MRI measures predict neurologic impairment at discharge. Multidimensional data-driven analytics (i.e., optimal-scaling-

transformed correlation, non-linear principal component analysis (NL-PCA)) were applied to explore the multivariate clustering among various MRI measures to determine their convergent validity and discriminant validity. Linear mixed modeling (LMM) was then applied to assess the relationship of these ensemble MRI measures with the degree of neurologic impairment measured by the American Spinal Injury Association (ASIA) Impairment Scale (AIS) at hospital discharge.^{36,37} The results provide evidence of face validity, convergent validity, discriminant validity, construct validity, and clinical predictive validity for multiple MRI measures when applied in acute thoracic SCI.

Materials and Methods

Study cohort

We performed an institutional review board and HIPAA compliant retrospective cohort study evaluating patients who presented to a Level I trauma center between 2005 and 2012 with acute thoracic or thoracolumbar SCI. Patients were identified using a Department of Neurological Surgery database compiled of patients with a principal diagnosis of SCI (International Classification of Diseases codes 952-957). Inclusion criteria were 1) age ≥ 18 years, 2) thoracic and/or lumbar spine MRI including at minimum sagittal and axial T2 imaging, and 3) documented clinical assessments including AIS at admission and discharge. Exclusion criteria were 1) surgical decompression and/or fusion prior to MRI, 2) MRI that was too degraded by motion or other artifact such that images were non-diagnostic as assessed by an attending neuroradiologist, 3) cervical spinal cord injury, and 4)

injuries primarily involving the conus medullaris or cauda equina nerve roots 5) pre-existing hardware. 25 patients met inclusion and exclusion criteria. Clinical data collected included patient age, gender, AIS grade at discharge, time to MRI, time to discharge, mechanism, and whether surgical decompression was performed prior to hospital discharge (Table 1). All patients in the study cohort had a principal diagnosis of SCI and underwent our institutional SCI treatment protocol. The 5 cases classified as AIS grade E on formal admission exam had documented symptoms of truncal/lower extremity sensory deficits and/or had documentation of motor weakness in the field. These deficits had resolved upon neurological examination on admission and therefore qualify as AIS grade E.

MRI

All MRI were acquired on a 1.5 Tesla GE Genesis Signa HDxt scanner, software version 15 (GE Healthcare, Milwaukee, WI). Routine trauma protocol thoracic spine MRIs were performed including at minimum sagittal T1 and T2 fast spin echo (FSE) sequences and axial T2 FSE sequences. For sagittal T1 imaging the following parameters were used; slice thickness=3mm, time to repetition (TR)= between 520ms and 630ms, time to echo (TE) = between 9ms and 15ms, echo train length (ETL) = 3, field-of-view (FOV)=30cm², acquisition matrix = 512 x 512. For sagittal T2; slice thickness, FOV and matrix size were as above with TR between 3100ms and 4000ms and TE between 105ms and 120ms and ETL between 19 and 21. For axial T2 imaging, slice thickness was 4mm, TR between 4000 and 4800ms, TE between 102 and 120ms, ETL =25, FOV = 18cm, and acquisition matrix size =

512 x 512. Additional sequences were performed but not evaluated for the purposes of this study.

Image Analysis

A board certified neuroradiologist and a neuroradiology trainee performed independent imaging ratings (Table 2), blinded to clinical outcomes, on retrospectively-evaluated imaging sequences (Figure 1). Any disagreements in categorization were discussed with ultimate deferral to the more experienced reader. The level of injury was defined as the epicenter of largest anterior to posterior extent of cord signal abnormality on sagittal imaging or as the level of bony injury/canal compromise if there was no cord signal abnormality. BASIC grading was performed as has been previously described (Figure 1D) by reviewing the axial images at the epicenter of the injury: Briefly, grade 0 injury represented normal spinal cord T2 signal, grade 1 injury represented T2 hyperintensity approximately confined to expected location of spinal gray matter, grade 2 injury represented T2 hyperintensity extending beyond the expected margins of central gray matter and obscuring gray-white margins but not involving the entire transverse extent of the spinal cord (a peripheral rim of normal appearing white matter was identified), grade 3 injury represented T2 hyperintensity involving the entire transverse extent of the spinal cord without any residual normal appearing white matter, and grade 4 injury represented grade 3 injury with superimposed discrete foci of intramedullary T2 hypointensity attributed to the presence of macroscopic intramedullary hemorrhage.⁴ All BASIC scoring was based upon a single axial image from the injury epicenter that was determined to have the most

severe grade among all axial slices. Sagittal grade was assigned as follows (Figure 1E): Grade 1 represented normal spinal cord signal; grade 2 represented T2 hyperintense intramedullary signal with longitudinal extent confined to a single vertebral level; grade 3 represented >1 vertebral level edema; and grade 4 represented mixed hemorrhage and edema.^{2, 3} We also measured the greatest longitudinal extent of injury on sagittal T2 images in mm as described in the SCI common data elements (CDE) version 1.0 (Figure 1A). MCC and MSCC were also both measured on mid-sagittal images as previously described, by dividing the anterior-posterior (AP) diameter of the canal (for MCC) and the AP diameter of spinal cord (for MSCC) by the average of the canal or spinal cord above and below as described in the literature with MCC measured on T1 and MSCC measured on T2 Figure 1B and 1C).^{11, 19, 27, 29, 38} TLICS was assigned as described in the literature after reviewing any necessary CT imaging and the clinical chart.³⁹⁻⁴¹

Multidimensional Analytical Workflow and Statistical Analysis

All statistical analyses were performed in SPSS v.22 (SPSS Inc.; Chicago, IL). To assess the relationship between the different MRI measures we used a NL-PCA in the general workflow depicted in Figure 2. NL-PCA is suitable for a set of variables including mixed measurement levels (nominal, ordinal and numeric).^{42, 43} In NL-PCA variables are assigned numerical values through an automated process called optimal scaling transformation. First, NL-PCA was applied using a 6 dimensional solution. The final dimensionality (i.e., number of principal components) of the PCA was defined based on 1) Kaiser rule: eigenvalue >1 and 2) Cattell rule: scree plot.^{44,}

⁴⁵ The NL-PCA was then pruned with reduced PC dimensions. To determine the

stability of the NL-PCA solution we performed a non-parametric balanced bootstrapping procedure using 2000 iterations and Procrustes rotation.⁴⁶ The 2 dimensional NL-PCA solution was further cross-validated with the bootstrapped solution by using root mean square difference in PC loading patterns, the coefficient of congruence, the Pearson product moment correlation coefficient and the Cattell salient variable similarity index. Convergence of these mathematically distinct metrics indicates consensus for replication of PC patterns. The sensitivity of the extracted 2 dimensional PC scores for predicting AIS at discharge was tested with a linear mixed model. To assess the bivariate relationship between AIS at discharge and MRI measures separate Spearman rank correlations and an optimal scaled regression were applied. These procedures allow a direct comparison between the univariate correlations from individual variables and multivariable sets with different metric features (i.e., ordinal and numeric). All predictive validity testing was based upon individual MRI measures from MRI obtained near time of admission and AIS at time of patient discharge from the hospital. Statistical significance for all analysis was set at $\alpha = 0.05$. Bootstrapping and power calculations indicated that the N=25 was sufficient for assessing the predictive validity of MRI with respect to AIS at discharge.

Levels of Validity

Validation of MRI measures involves different levels of validity assessment as described by classical measurement theory. 'Face validity' is defined as the concept that the MRI measures accurately reflect what they purport to measure on face value (i.e. an MRI-measured lesion looks like a lesion). 'Convergent validity' is

the concept that measures that should correlate, do indeed correlate (i.e., lesion length and lesion area do correlate). 'Discriminant validity' refers to the concept that measures that should diverge, do indeed diverge (i.e. measures of ligamentous change diverge from neuroanatomical measures). 'Construct validity' refers to the concept that multidimensional patterns are coherent from a theoretical perspective (i.e. neuroscores coalesce as coherent unit). Construct validity can be considered to involve both discriminant and convergent validity. 'Predictive validity' refers to the concept that a multidimensional MRI patterns can predict outcome. In the results section we address which level of validity is addressed by each statistical finding.

Results

Patient characteristics, MRI metrics, and TLICS scores for our cohort are presented in Table 1. Optimally-scaled correlation revealed strong bivariate associations among MRI measures (Figure 3A). NL-PCA analysis revealed that PC1-3 had high loadings by MRI scores (Figure 3B). The Cattell and Kaiser criteria for PC retention converged on retention of a pruned 2-dimensional PC solution (Figure 3C). Re-extraction of NL-PCA restricted to 2-dimensions confirmed that PC1-2 accounted for 87.0% of the variance (64.3% and 22.7%, respectively) in imaging findings (Figure 3D). The bootstrapping results support the stability of the 2 dimensional PCA solutions with only marginal changes in the total variance accounted for (total: 89.4%, PC1: 64.3%, PC2: 25.1%). Further, the loading pattern of the 2 dimensional NL-PCA strongly agrees with the loading pattern of the

bootstrapped PCA solution for both PC1 (root mean square difference=0, coefficient of congruence=1, Pearson product moment correlation coefficient=1 and Cattell salient variable similarity index=1, $p < .05$) and PC2 (root mean square difference=0, coefficient of congruence=1, Pearson product moment correlation coefficient= 1 and Cattell salient variable similarity index= 0.86, $p < .05$). In the 2 dimensional NL-PCA solution all imaging variables loaded positively on PC1. MCC, MSCC, and TLICS also loaded positively on PC2 (variance orthogonal to PC1) while BASIC, sagittal grade, and longitudinal extent of injury loaded negatively on PC2. Together these results suggest that: the PC1-2 reflect radiological tissue changes (face-validity); that PC1 reflects agreement among MRI scoring schemes (convergent validity); and that PC1 and PC2 reflect distinct patterns, with PC2 reflecting divergence among 2 distinct blocks of scoring schemes (discriminant validity).

To better understand the discriminant nature of PC2 we projected individual patients into the PC1-PC2 biplot space (Figure 4) and discovered that there appeared to be a broad dispersion of subjects within the PC space, suggesting the potential for distinct subpopulations. We hypothesized that spinal decompression surgery may account for the dissociations among patient distributions. Linear mixed model regression confirmed that spinal decompression impacted PC2 scores ($F = 25.4$, $p < .0001$) but not PC1 ($p > .05$). This suggests that PC2 may reflect MRI features associated with the clinical decision making process to perform spinal cord decompression. Careful re-examination of the loadings, further supports this idea (see Figure 3D).

To test the predictive validity of PC1 and PC2 MRI ensembles, we used mixed model regression to test their association with AIS at discharge. Both PC1 and PC2 were statistically significantly related to AIS at a discharge (PC1: $F=8.63$, $p=0.001$, $\eta^2=0.55$, $\text{power}=0.98$; PC2: $F=3.28$, $p=0.041$, $\eta^2=0.32$, $\text{power}=0.66$). PC1 specifically predicted AIS neurological impairment at time of patient discharge across the range of injuries in a monotonic fashion, with higher PC1 scores reflecting worse function (AIS A), and lower PC1 scores reflecting better function (AIS E) ($p < .05$ by linear contrast; $p > .05$ for quadratic). PC2 on the other-hand had a narrower range of association with neurologic impairment, differentiating AIS A from other AIS grades ($p < .05$) with no other statistical significance. Due to the retrospective nature of the study AIS at discharge was chosen as the short-term outcome. To assess the relationship between PC1/ PC2 and length of stay a Pearson correlation was performed (PC1: Pearson $r=0.45$, $p=0.023$ and PC2 $r=-0.39$, $p=0.057$) this indicates that multidimensional MRI predicts length of stay, as a secondary validation endpoint.

To better understand the predictive validity of the individual MRI scores vs. the PC1 and PC2 ensembles, we performed a non-parametric Spearman rank correlations of imaging variables with AIS at discharge (Table 3 and Figure 5). BASIC score ($\rho=-0.93$), sagittal grade ($\rho=-0.85$), longitudinal extent of injury ($\rho=-0.83$), and PC1 ($\rho=-0.75$) were all negatively correlated with AIS at discharge. PC2 ($\rho=0.49$) was mildly positively correlated with AIS at discharge, while TLICS, MCC, and MSCC were not statistically significantly correlated with AIS at discharge. To confirm the comparative predictive validity results we used an

optimal scaled regression. This method provides a way to compare correlations between variables with different properties and distributions. BASIC was the only statistically significant ($p=0.001$) predictor of AIS at discharge in this multiple variable model. Due to multicollinearity PC1 and PC2 were not included in the optimal scaling regression.

Discussion

In this study we assessed multiple MRI metrics of SCI, which were all predominately developed for use in the more common cervical SCI, here applied in thoracic SCI. TLICS, which is a injury classification system for surgical decision making in thoracic spinal column injury and not a prognostic system, was also included in order to evaluate its relationship with the other imaging variables. It should be noted that TLICS does incorporate clinical data related to patient neurologic status in addition to imaging findings. We used non-linear principal components analysis to characterize the relationships of these variables and found two principal components accounting for 87.0% of the variance. All imaging variables loaded positively on PC1 (64.3% of the variance), which was highly related to AIS at discharge. MCC, MSCC, and TLICS also loaded positively on PC2 (22.7% of the variance) while variables concerning spinal cord signal abnormality loaded negatively on PC2. We found that PC2 was highly related to the patient undergoing surgical decompression. BASIC, sagittal grade, and longitudinal extent of signal abnormality were all negatively correlated with AIS at discharge with the highest individual level of correlation for BASIC. In a multiple variable model BASIC was the

only statistically significant predictor of AIS at discharge, demonstrating that it most accurately predicted the variance of AIS at discharge in our study population. Our study provides evidence of convergent validity, construct validity, and clinical predictive validity for these imaging predominant measures of SCI when applied in acute thoracic SCI.

Variables involving spinal cord signal abnormality are highly related to each other and to AIS at discharge. By definition these three variables are similar as they primarily consider the presence or absence of T2 signal hyperintensity in the spinal cord. The axial grading system (BASIC) and the sagittal grading system differ in their mild to moderate grades and direction of significance, however both consider hemorrhage superimposed on edema as the highest grade. Otherwise in the mild to moderate grades, BASIC is primarily concerned with the degree of spared white matter and the sagittal grading system is primarily concerned with single vertebral level vs. multiple vertebral level edema. The sagittal grading system (ordinal) and the longitudinal extent of T2 signal abnormality (numerical) are by definition similar concepts except that the sagittal grade also accounts for the presence of hemorrhage. As expected these variables grouped together on principal components analysis and were positively correlated together providing evidence of convergent and construct validity, and were negatively correlated with AIS at discharge providing evidence of clinical predictive validity. BASIC demonstrated the highest individual degree of negative correlation with AIS at discharge, however all three metrics can be considered individually valid for predicting early neurological impairment in thoracic SCI. The multiple variable model identified BASIC as the

dominant imaging variable in predicting AIS at discharge, as it was the only statistically significant variable in the multiple regression model. This suggests that BASIC (a brief ordinal scale) most tightly captures AIS (also a brief ordinal scale) at discharge compared to the other measures.

MCC, MSCC, and TLICS grouped together with the other imaging variables on PC1 but diverged from the other imaging variables (of spinal cord signal abnormality) on PC2. As PC2 was highly related to the patient undergoing spinal decompression and positively correlated with AIS at discharge, the relationship of these variables that loaded positively on PC2 (MCC, MSCC, TLICS) with AIS at discharge is thus quite complex. These three variables have variance with PC1 correlating negatively with AIS at discharge, and variance with PC2 correlating positively with AIS at discharge and being highly related to the likelihood of undergoing surgical decompression. PC2 thus may capture some of the nuances of surgical decision-making reflected in TLICS whereby an incomplete SCI at admission receives a higher individual scoring than a complete SCI. The particular phenotype captured by a high PC2 score would be a patient with a high MCC, MSCC, and TLICS but lower scores on measures of cord signal abnormality; a patient with an unstable spine and compression but a relatively preserved spinal cord. The fact that MCC and MSCC did not individually have a significant correlation with AIS at discharge is consistent with previous literature examining measures of spinal canal stenosis with thoracolumbar SCI outcomes and may reflect the complexity of their relationship with both surgical decision-making and subsequent early neurological impairment.⁴⁷ The strong negative correlations between direct MRI measures of SCI

(BASIC score, sagittal grade, and longitudinal length of T2 signal hyperintensity) and clinical outcomes suggests incorporation of these measures into surgical decision making tools may be helpful. Defining valid imaging biomarkers for thoracic and thoracolumbar SCI is critically important as the thoracic spinal cord has been proposed as the most suitable region for initial invasive clinical trials targeting SCI.^{48, 49}

Our study has several limitations mostly related to the retrospective technique and relatively small sample size. Our retrospective technique allowed us to effectively study the relatively rare thoracic SCI in an efficient manner but did limit the clinical variables to those already collected in routine clinical care. The retrospective nature of this study also limits our control over timing of MRI after injury. Leypold and colleagues have shown that the longitudinal extent of T2 hyperintensity can increase by up to 1 vertebral body height per day in the acute stage of injury⁵⁰. Our institution routinely obtains MRI early after injury and 88% (22/25) were performed within 24 hours of injury, thus limiting the effect of delayed timing on extent of T2 hyperintensity. Future prospective controlled experiments would ideally control for variables such as hemodynamic support, timing of surgical decompression, steroid therapy, and timing of MRI after injury with longer-term clinical follow up and a larger number of patients. Importantly, our study does suggest that any prospective collection of data in thoracic SCI should include metrics of spinal cord signal abnormality on MRI as measured in this study.

Another limiting factor is the use of AIS grade as fairly coarse primary outcome measure for thoracic SCI in our cohort. Due to the retrospective nature of

this study, more granular outcome measures, such as functional independence measure (FIM), were not available for analysis. Although the significance of AIS grade has been questioned in thoracic SCI, Lee and colleagues recently showed that AIS grade changes are associated with significant functional benefit relative to FIM scores and ambulation in a retrospective analysis of a large longitudinal database of thoracic SCI patients.^{51, 52}

It should be noted that structural MRI findings correlated with early impairment with varying resolution, depending on the scoring scheme (e.g., BASIC vs. sagittal grade). Multiple regression analysis confirmed that most of the univariate MRI assessments were noisy correlates of functional impairment, with the sole exception of the BASIC score. In testing theory, this class of evidence is referred to as 'predictive validity', and it directly addresses whether a set of measurements (MRI features) have value for predicting a separate outcome domain (AIS grade) at a later time.

Our application of NL-PCA directly assessed whether the multidimensional ensemble of spinal cord MRI features performs better than each individual outcome. It should be noted that the NL-PCA is a rigorous and appropriate approach for performing multivariate pattern-detection to compare the relative merits of multiple scales that purport to measure the same underlying features (in this case structural MRI features). This approach has a long history in physics, human performance testing, and other disciplines dating back over a century.^{53, 54} Although it is currently unusual to have such advanced analytics applied in the clinic, applications like the one here promise to be a central feature of

the emerging field of 'precision medicine', where analytics will be integrated in clinical decision making.^{55, 56} Accordingly several very recent papers incorporate NL-PCA as a precision medicine tool in both preclinical and clinical SCI.⁵⁷⁻⁵⁹ The present findings suggest that multidimensional MRI features of thoracic spinal cord may have relevance for clinical issues such as patient stratification for diagnosis, intervention planning, and clinical trial criteria. However, further work is required to test the capacity of structural MRI to predict long-term outcome.

In conclusion, this study validates the use of BASIC and other MRI measures of acute SCI specifically in the setting of thoracic SCI. Principal component analysis identified two distinct patterns of variance, PC1, which was highly related to AIS at discharge, and PC2, which was highly related to surgical decompression. The highest individual correlation with AIS at discharge was seen with the BASIC system although all metrics of spinal cord signal abnormality had a high degree of individual negative correlation with AIS at discharge. The relationship of MCC and MSCC with AIS at discharge was found to be more complex, likely reflecting the use of these metrics along with TLICS in surgical decision-making. A multiple variable regression model identified BASIC as the only statistically significant predictor of AIS at discharge, signifying that BASIC best captured the variance in AIS within our study population.

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Disclosures

Member of the data monitoring committee for StemCells, Inc. (JFT); ad hoc consultant for Acorda Therapeutics (ARF).

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Figure legends

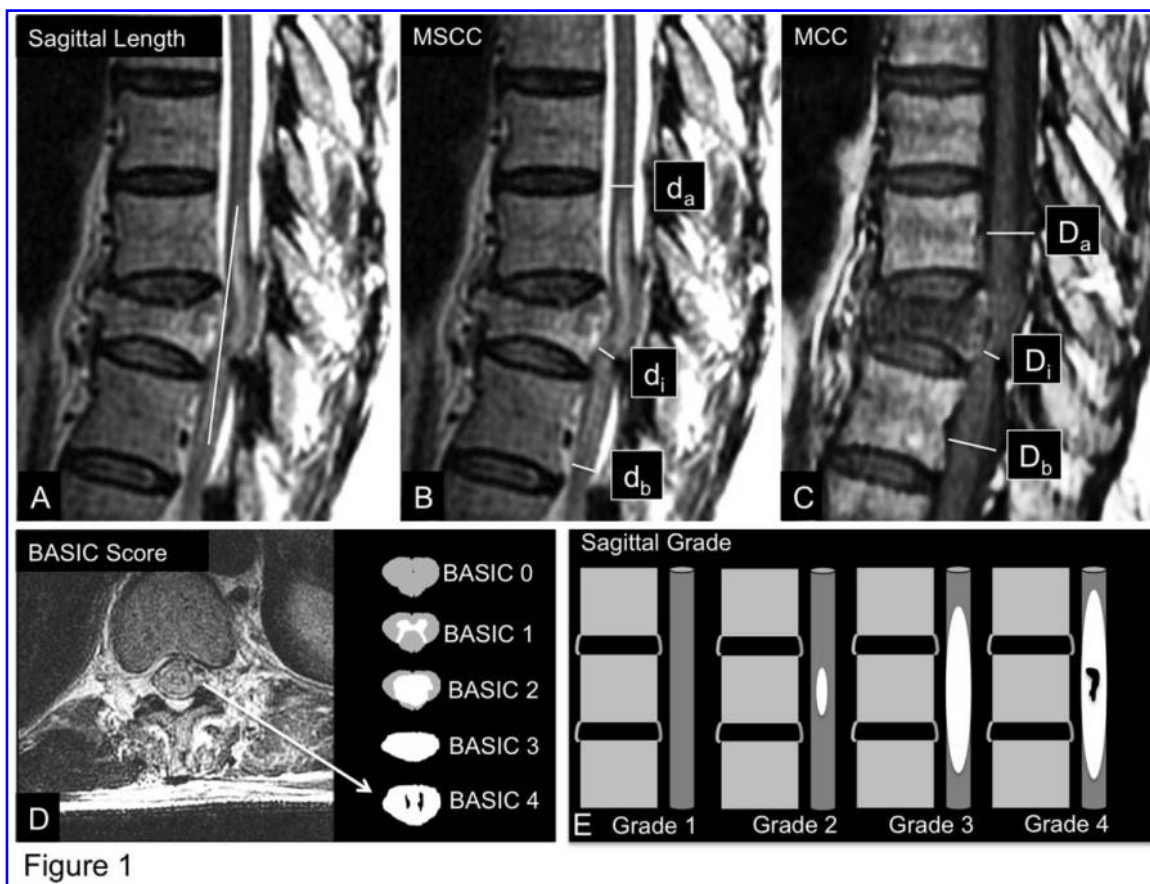


Figure 1

Figure 1. Image analysis. A and B) Sagittal T2-weighted MRI of the thoracic spine in an acute SCI patient demonstrating how this sequence was used to measure the length of T2 signal hyperintensity in mm (white line in A), and to calculate MSCC (B, $(1-(d/((d_a+d_b)/2))) \times 100\%$). C) Sagittal T1-weighted image of the thoracic spine demonstrating how this sequence was used to measure MCC ($(1-(D/((D_a+D_b)/2))) \times 100\%$). D) Axial T2-weighted MRI of the thoracic spine at the level of the epicenter of injury in a different patient. Foci of T2 hypointense hemorrhage are surrounded by hyperintense edema with no normal cord signal, consistent with BASIC grade 4; white arrow denotes associated cartoon depiction of BASIC axial grade. E) Cartoon of the sagittal grading system. BASIC, Brain and Spinal Injury Center score; Sag, Sagittal; MCC, maximum canal compromise; MSCC, maximum spinal cord compression.

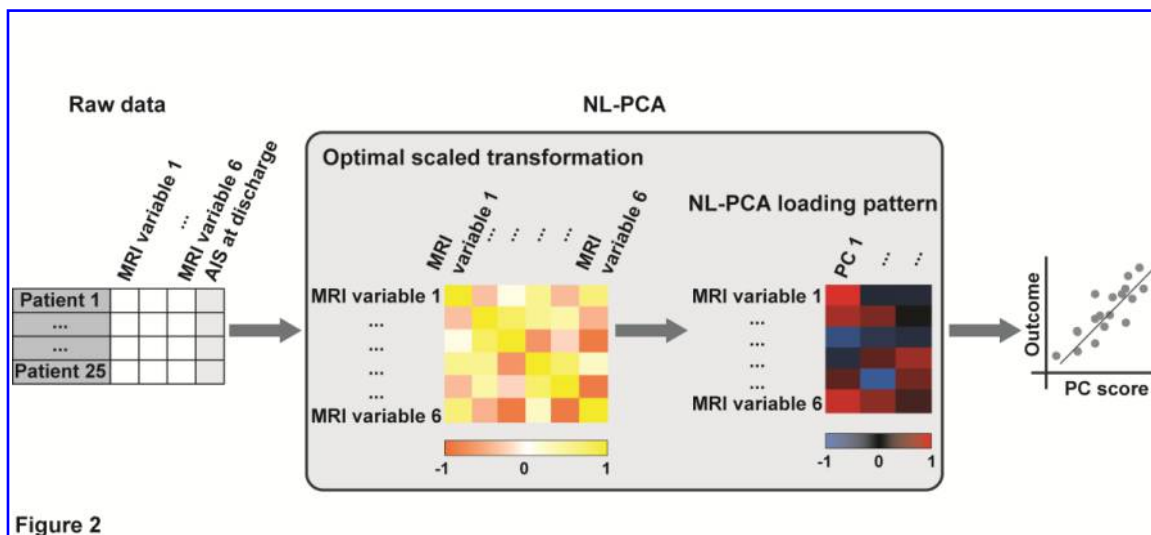


Figure 2

Figure 2. Multidimensional analytical workflow. Raw MRI variables are fed into a NL-PCA. NL-PCA uses a process called optimal scaling transformation to handle different analysis levels (e.g. ordinal and numeric) in the dataset. Optimal scaling assigns quantitative values to categorical variables optimally, meaning maximizing the variance of the predefined number of PC (i.e., dimensions). The NL-PCA loading pattern shows the weight (i.e., loading) of every single MRI variable on the extracted PCs. In a next step individual PC scores are used to define the predictive nature of PCs on outcome. An individual PC score is the sum of the multiplied loadings by the individual raw value of every single variable. PC, principal component; NL-PCA, non-linear principal component analysis.

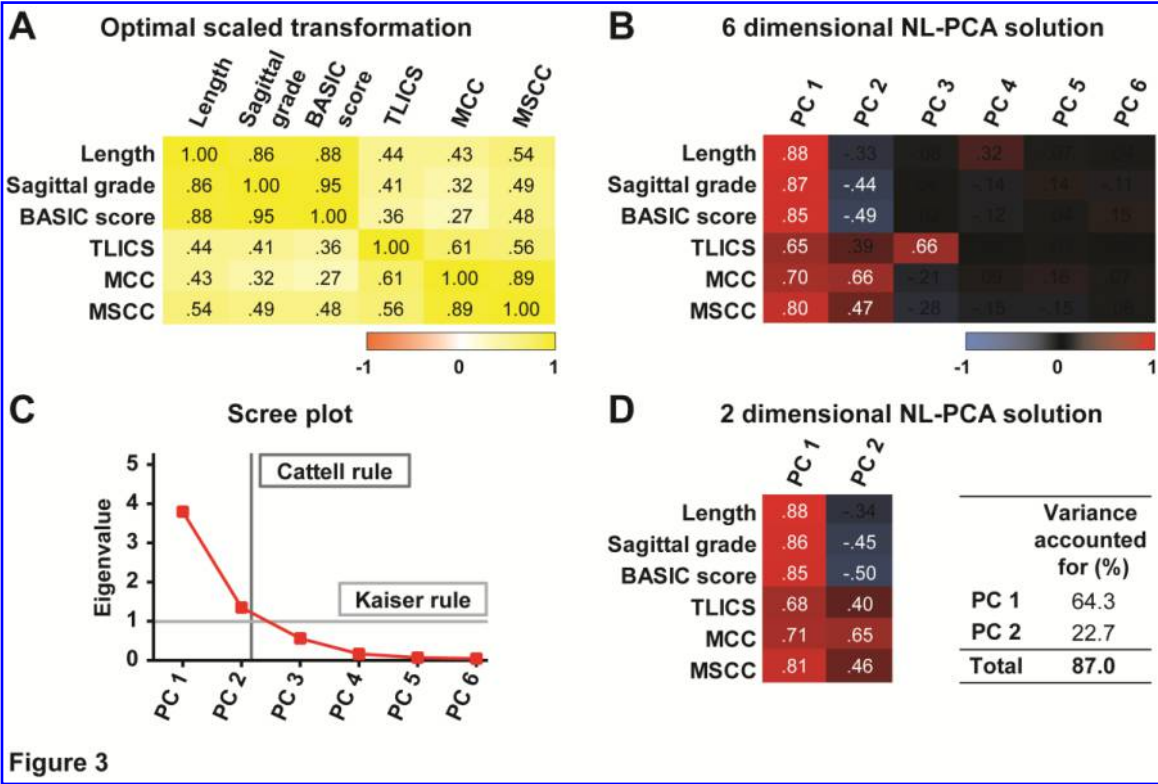


Figure 3

Figure 3. NL-PCA results demonstrate face validity, convergent validity, and construct validity. A) Optimal scaled transformation matrix of all MRI measures. B) 6 dimensional NL-PCA solution loading patterns. Loadings $>|0.4|$ are emphasized in white. C) Shows the screeplot for the 6 dimensional NL-PCA. The Cattell and the Kaiser rule were applied to define the amount of components to retain for the final NL-PCA. The criteria converged on a 2-dimensional solution D) Shows the re-extracted 2 dimensional NL-PCA solution and the amount of variance accounted for by the two PCs. Loading values $>|0.4|$ are in white text. BASIC score, Brain and Spinal Injury Center score; MCC, maximum canal compromise; MSCC, maximum spinal cord compression; NL-PCA, non-linear principal component analysis; PC, principal component; TLICS, thoracolumbar injury classification system.

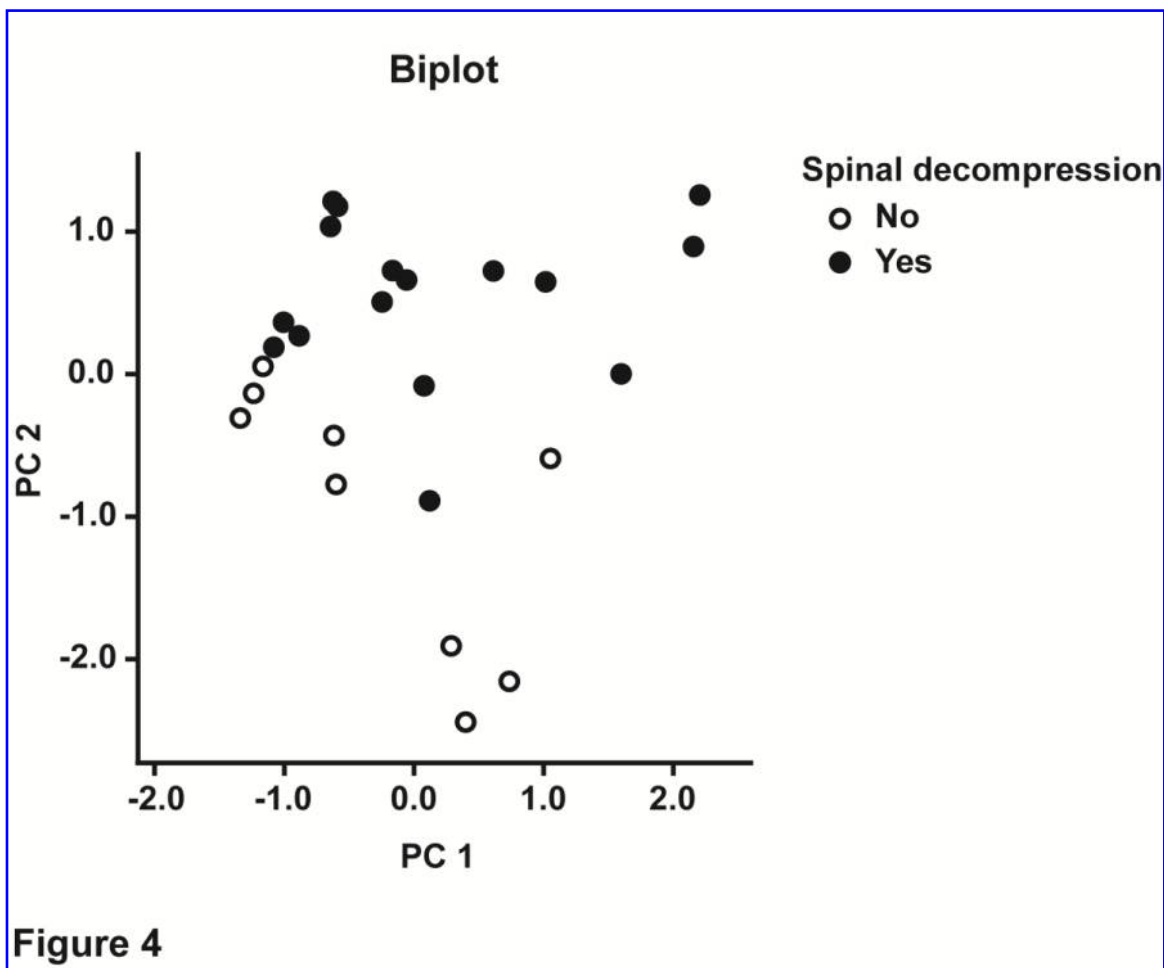


Figure 4

Figure 4. Discriminant validity of PC2. Individual subject's PC scores are plotted into the 2D biplot space described by PC1 and PC2. Subjects that underwent surgical decompression (closed circles) after MRI image acquisition have higher PC2 scores than those who did not (open circles). The biplot highlights the discriminative validity of PC2. PC, principal component.

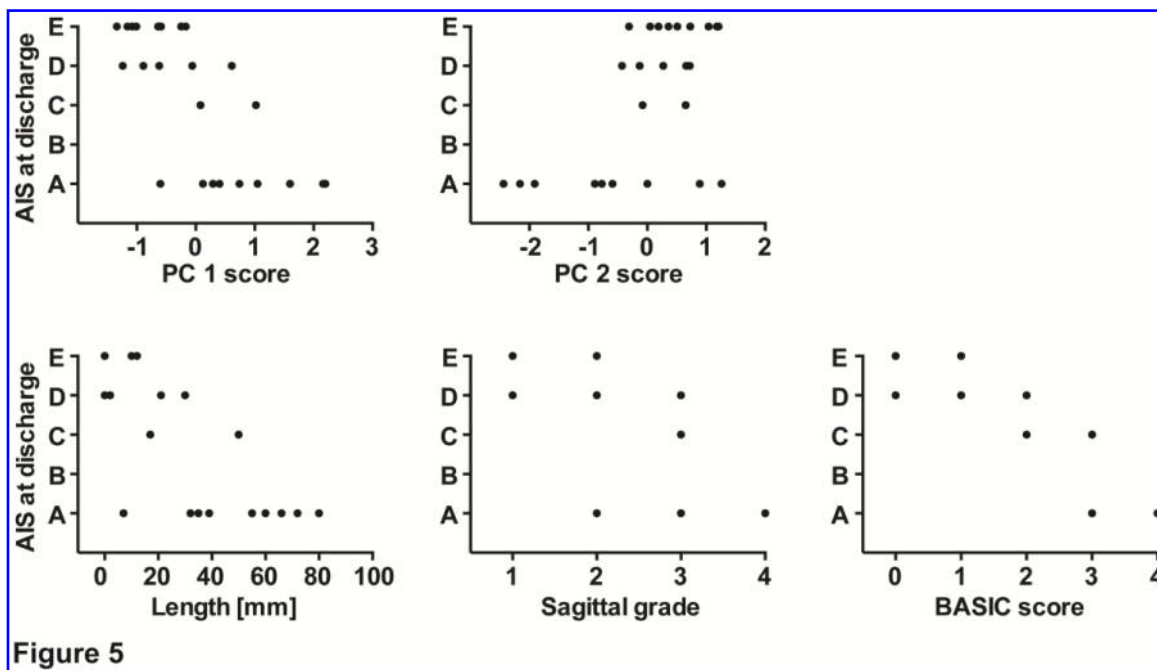


Figure 5. Predictive validity. Scatterplots of AIS at discharge with each statistically significant variable. BASIC score had the highest individual level of individual correlation with AIS at discharge. BASIC score ($\rho=-0.927$), sagittal grade ($\rho=-0.852$), longitudinal extent of injury ($\rho=-0.825$), and PC1 ($\rho=-0.753$) were all negatively correlated with AIS at discharge. PC2 ($\rho=0.486$) was mildly positively correlated with AIS at discharge, while TLICS, MCC, and MSCC were not statistically significantly correlated with AIS at discharge. Note, that due to the ordinal scale of the sagittal grade and the BASIC score a number of subjects coincide on both x- and y-axes. AIS, American Spinal Injury Association Impairment Scale; PC, principal component. BASIC score, Brain and Spinal Injury Center score; MCC, maximum canal compromise; MSCC, maximum spinal cord compression; TLICS, thoracolumbar injury classification system.

Tables

Table 1. Patient Characteristics. Results are expressed as N or mean \pm standard deviation.

Patient Characteristics	
Age (years)	38.32 \pm 15.74
Gender	17 Male: 8 Female
Injury Type	Blunt=21, Penetrating=4
AIS at Admission	A=11, B=2, C=1, D=6, E=5
AIS at Discharge	A=9, B=0, C=2, D=5, E=9
Time to MRI (hours)	14.68 \pm 18.56
Time to Discharge (days)	20.96 \pm 21.48
Surgical Decompression Prior to Discharge	Yes=16, No=9
Mechanism of Injury	10 Fall from height, 5 motor vehicle collision, 3 crush injuries by large falling objects, 2 gun shot wounds, 2 stab wounds, 1 motorcycle collision
Vertebral Body Level of Epicenter of Injury by Imaging	1 T2, 1 T3, 1 T4, 3 T6, 2 T7, 3 T8, 2 T9, 1 T11, 7 T12, 3 T1, 1 without detectable injury
BASIC Score	1.88 \pm 1.67
Sagittal Grade	2.32 \pm 1.22
Longitudinal Extent of Injury (mm)	23.52 \pm 26.56
TLICS Score	5.16 \pm 2.78
MCC (%)	23.38 \pm 27.36
MSCC (%)	18.67 \pm 24.02)

Table 2. MRI scoring schemes

Brain and Spinal Injury Center grading system	Ordinal	0-4; 0=normal, 1=gray matter only, 2=some WM, 3=all WM in plane, 4=with hemorrhage.
Sagittal grade	Ordinal	1-4; 1=normal, 2=less than a vertebral body (VB), 3=longer than one VB, 4=with hemorrhage.
Longitudinal extent of T2 signal abnormality	Numerical	[mm]
Thoracolumbar injury classification system (TLICS)	Ordinal	Rates: morphology (1-4), neurologic status (0-3), and integrity of the posterior ligamentous complex (0-3).
Maximum canal compromise (MCC)	Numerical	$MCC(\%) = 1 - [D_x / (D_a + D_b) / 2] \times 100\%$; D: canal width
Maximum spinal cord compression (MSCC)	Numerical	$MSCC(\%) = 1 - [d_x / (d_a + d_b) / 2] \times 100\%$; d: spinal cord width

Table 3. Spearman rank correlation and optimal scaling regression to predict AIS at discharge. Length of signal abnormality, sagittal grade, BASIC score, and PC1 are all negatively correlated with AIS at discharge while PC2 is positively correlated with AIS at discharge. Optimal scaling regression identified BASIC score as the only statistically significant variable in this multiple variable model to predict AIS at discharge.

	Spearman correlation			Optimal scaling regression			
	Rho	Rho squared	Sig	Zero-order	Partial	Part	Sig
Length	-0.83	0.68	<0.001	-0.81	-0.09	-0.02	0.859
Sagittal grade	-0.85	0.73	<0.001	-0.67	0.65	0.16	0.514
BASIC score	-0.93	0.86	<0.001	-0.96	-0.92	-0.44	0.001
TLICS	-0.21	0.04	0.323	-0.11	-0.64	-0.15	0.203
MCC	-0.04	0.00	0.850	-0.17	0.30	0.06	0.405
MSCC	-0.20	0.04	0.351	-0.40	0.06	0.01	0.862
PC1	-0.75	0.57	<0.001				
PC2	0.49	0.24	0.014				

Complications and outcomes of vasopressor usage in acute traumatic central cord syndrome

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OBJECT The optimal mean arterial pressure (MAP) for spinal cord perfusion after trauma remains unclear. Although there are published data on MAP goals after spinal cord injury (SCI), the specific blood pressure management for acute traumatic central cord syndrome (ATCCS) and the implications of these interventions have yet to be elucidated. Additionally, the complications of specific vasopressors have not been fully explored in this injury condition.

METHODS The present study is a retrospective cohort analysis of 34 patients with ATCCS who received any vasopressor to maintain blood pressure above predetermined MAP goals at a single Level 1 trauma center. The collected variables were American Spinal Injury Association (ASIA) grades at admission and discharge, administered vasopressor and associated complications, other interventions and complications, and timing of surgery. The relationship between the 2 most common vasopressors—dopamine and phenylephrine—and complications within the cohort as a whole were explored, and again after stratification by age.

RESULTS The mean age of the ATCCS patients was 62 years. Dopamine was the most commonly used primary vasopressor (91% of patients), followed by phenylephrine (65%). Vasopressors were administered to maintain MAP goals for a mean of 101 hours. Neurological status improved by a median of 1 ASIA grade in all patients, regardless of the choice of vasopressor. Sixty-four percent of surgical patients underwent decompression within 24 hours. There was no observed relationship between the timing of surgical intervention and the complication rate. Cardiogenic complications associated with vasopressor usage were notable in 68% of patients who received dopamine and 46% of patients who received phenylephrine. These differences were not statistically significant (OR with dopamine 2.50 [95% CI 0.82–7.78], $p = 0.105$). However, in the subgroup of patients > 55 years, dopamine produced statistically significant increases in the complication rates when compared with phenylephrine (83% vs 50% for dopamine and phenylephrine, respectively; OR with dopamine 5.0 [95% CI 0.99–25.34], $p = 0.044$).

CONCLUSIONS Vasopressor usage in ATCCS patients is associated with complication rates that are similar to the reported literature for SCI. Dopamine was associated with a higher risk of complications in patients > 55 years. Given the increased incidence of ATCCS in older populations, determination of MAP goals and vasopressor administration should be carefully considered in these patients. While a randomized control trial on this topic may not be practical, a multiinstitutional prospective study for SCI that includes ATCCS patients as a subpopulation would be useful for examining MAP goals in this population.

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KEY WORDS ATCCS; central cord; traumatic spinal cord injury; cervical spine; spinal cord perfusion; vasopressors; dopamine; trauma

ABBREVIATIONS AANS/CNS = American Association of Neurological Surgeons and Congress of Neurological Surgeons; ASIA = American Spinal Injury Association; ATCCS = acute traumatic central cord syndrome; ICU = intensive care unit; ISP = intraspinal pressure; MAP = mean arterial pressure; SCI = spinal cord injury; SCPP = spinal cord perfusion pressure.

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DISCLOSURE Dr. Dhall reports receiving speaking honoraria from DePuy and Globus.

SINCE Schneider colleagues' well-known description of acute traumatic central cord syndrome (ATCCS) in 1954, significant research has focused on the management of these cases.¹⁸ In recent years, there has been an increased focus on ATCCS, as this represents the most common form of incomplete spinal cord injury (SCI).³ Additionally, ATCCS complications have been shown to increase in elderly patients.¹⁴ As the US population ages, expanding knowledge of ATCCS will only become more important. Given the potentially debilitating nature of these injuries, and their impact on our society, it is important to explore the medical and surgical management of ATCCS.⁵

Many recent studies on SCI and ATCCS have focused on the timing of surgical intervention and decompression and report mixed results, all citing the need for additional prospective studies.^{19,24,26} These studies, along with recent prospective investigations, suggest that early surgical intervention (decompression within 24 hours of SCI) may improve long-term prognosis.^{2,9,24} While the focus on surgical decompression, efficacy, and timing is an important aspect of ATCCS management, little focus has been placed on medical management and perfusion for these patients.²

As part of the medical management of SCI, there has been an increased focus on vasopressor utilization. Previous studies have linked vasopressor support to improved outcomes, but recognized that there are no validated protocols for the implementation of these interventions.^{15,21} The 2013 American Association of Neurological Surgeons and Congress of Neurological Surgeons (AANS/CNS) guidelines for cervical SCI treatment recommended raising the mean arterial blood pressure of acute SCI patients to the range of 85–90 mm Hg, while acknowledging that further research should be conducted to formulate consistent guidelines and protocols.^{2,17} As this recommendation was made primarily based on a single, large, retrospective study with significant positive results, the AANS/CNS author group encouraged more robust research as it relates to the medical management of cervical SCI subpopulations.

Concurrently with ongoing research investigating vasopressor utilization for traumatic SCI, poor clinical outcomes have been reported in the setting of early vasopressor use for critically injured, nonneurosurgical, trauma patients.¹⁶ Excluding traumatic brain injury and SCI, Plurad et al. found a significant, fluid status-independent association between early vasopressor administration and mortality.¹⁶ In the setting of septic shock and cardiogenic shock, other studies found that dopamine was associated with significantly higher complication rates and mortality when compared with norepinephrine.^{6,7} To the best of our knowledge, no previous studies have evaluated the role and potential risks of vasopressor utilization specifically in ATCCS patients. Due to the frequency of ATCCS, and its increased incidence in the aging population, research related to the medical management of these patients has become increasingly important, particularly in light of the current lack of universal standards.^{2,3,14,17} In this study, we explored the ATCCS subpopulation of acute SCI in order to establish a better understanding of perfusion pressure management in an effort to complement ongoing research

related to surgical timing and decompression, and to provide a detailed analysis of complications in these injuries.⁹ Additionally, we hypothesized that specific vasopressors may be linked to higher complication rates, along the lines of recent research on critical trauma and shock.^{6,7,12}

Methods

This study was reviewed and approved by the Committee on Human Research at the University of California, San Francisco, with an exemption from individual patient consent. We performed this retrospective cohort study of patients at a single Level 1 trauma center and created a database for analysis in REDCap (Research Electronic Data Capture), which was hosted at the University of California, San Francisco, in order to maintain data security and validity.

Population Selection

Potential study participants were identified by querying a preexisting database maintained by the Department of Neurological Surgery, which included all sequential patients with a principal diagnosis of SCI (ICD code: 953–957) from 2005–2011. This database includes 131 patients who met the following criteria: 1) age \geq 18 years; 2) presence of SCI; 3) admission to the intensive care unit (ICU); and 4) received vasopressors to meet mean arterial pressure (MAP) goals for greater than 24 hours. For this study, we had the specific additional inclusion criteria of the presence of central cord syndrome, as defined by the 2013 AANS/CNS guidelines for the management of ATCCS.² From this subpopulation, an additional comprehensive chart review was conducted to elucidate a better understanding of the injury and its management.

Population Characteristics, Complications, and Outcomes

The following variables were collected from the Department of Neurological Surgery database: sex, age, year of injury, vasopressor administration (type and duration of administration), American Spinal Injury Association (ASIA) grade on admission and discharge, level of SCI, and characteristics of injury. These data were then expanded by a blinded researcher by adding variables, including trauma characteristics, administration of methylprednisolone or other steroids, hospital length of stay, ICU length of stay, and surgical interventions. These data were collected from all aspects of the chart, including discharge summaries, nursing notes, progress notes, consent for procedures, operative reports, rehabilitation notes, and pharmacy records. The blinded researcher also independently verified the original data obtained from the departmental database.

Another researcher also reviewed the complications. These included surgical infections, wound complications, hospital-acquired infections, respiratory failure, hemodynamic complications, and cardiogenic complications. Cardiogenic complications included elevated troponins, atrial fibrillation, ventricular tachycardia, significant tachycardia (heart rate $>$ 130 bpm), and significant bradycardia (heart rate $<$ 50 bpm). Additionally, invasive procedures—including intubation, tracheostomies, gastrostomies, arterial

line placement, central line placement, and peripherally inserted central catheters—were reviewed as indicative of advanced medical care. Outcomes were determined based on improvement in neurological function, as indicated by the ASIA grade from admission to discharge and/or death. ASIA grade was selected as the measure of neurological function, given the recommendations of the AANS/CNS guidelines for the classification of cervical injuries and significant validation for the prognostic value of the ASIA grade.^{10,13,25}

Statistical Analysis

Descriptive statistics were used to examine the complications associated with vasopressor administration in ATCCS patients. All statistical analyses were performed using SPSS statistical analysis software (IBM SPSS Statistics for Macintosh, version 22.0). For all univariate analyses, the continuous variables are presented as the means with corresponding standard deviations. The univariate descriptions of the categorical data are presented as the incidence and associated percentages. Complications associated with the administration of the 2 primary vasopressors—dopamine and phenylephrine—were compared utilizing the chi-square and Fisher exact tests. Given the high incidence of ATCCS in older patients, an additional subanalysis was performed between patients older and younger than 55 years, which is an age cutoff point based on the recent literature on vasopressors.¹⁶ These groups were further compared using the Pearson chi-square test for dichotomous variables and 2-tailed t-tests for continuous data. For all statistical comparisons, statistical significance was defined as $p \leq 0.05$. The odds ratios were calculated for all cross-tabulated descriptive statistics with accompanying 95% confidence intervals.

Results

Cohort Description and Management

Of the 131 patients in the original database, 34 were determined to have ATCCS, as defined by the inclusion criteria, with complete records available for analysis. As shown in Table 1, 28 (82%) were male and 6 (18%) were female with a mean age of 61.53 ± 16.33 years. The average hospital length of stay was 18.64 ± 19.09 days with an average of 11.67 ± 13.73 days of care in the ICU. The acute SCI methylprednisolone protocol was administered to 20 patients (59%), while 14 patients (41%) were determined to be ineligible for the steroid protocol based on the decisions of their managing surgeon. Chart review indicated that methylprednisolone was not administered for multiple reasons, including medical comorbidities, injury severity, surgeon preference, and timing outside of the initial window of therapeutic intervention. Patients who did not receive steroids presented with more severe injury when compared with the group that received steroids, as indicated by higher average Injury Severity Scores (28 vs 21, respectively), but this did not reach significance ($p = 0.353$). There was no statistical difference in cardiogenic complications between patients who received or did not receive steroid protocols (85.0% for patients who received steroids [17 of 20] vs 64.29% for patients who did not re-

TABLE 1. Descriptive demographics*

Variable	Value
No. of patients	34
Male	28 (82.35)
Female	6 (17.65)
Mean age (yrs)	61.53 ± 16.33
Mean MAP goals >85 mm Hg (hrs)	100.78 ± 47.54
Mean ISS	23.52 ± 17.91
Steroids administered	20 (58.82)
No steroids	14 (41.18)
Surgery in <24 hrs	16 (47.06)
Surgery in >24 hrs	9 (26.47)
No surgery	9 (26.47)
ASIA grade improvement	19 (55.88)
No ASIA grade improvement	15 (44.12)
Mean ICU LOS (days)	11.67 ± 13.73
Mean hospital LOS (days)	18.64 ± 19.09
Mortality	2 (5.88)

ISS = Injury Severity Score; LOS = length of stay.

* Continuous variables are reported as the mean \pm SD; categorical variables are reported as number (%).

ceive steroids [9 of 14]; OR with steroids 3.142 [95% CI 0.608–16.289], $p = 0.161$). Additionally, when comparing the steroid group to the nonsteroid group, there were no statistical differences in any of the measured complication rates or outcomes. Decompressive surgery was performed in the first 24 hours in 16 patients (47%). Surgical intervention after 24 hours was noted in an additional 9 patients (26%), with the remaining 9 patients having no surgical intervention. Those patients who did not have surgical intervention either elected against the procedure, were medically unstable to the extent that the risks outweighed the benefits, or saw improvement without decompression. Of the patients who underwent decompressive surgery, 64% (16 of 25 patients) underwent surgery within the first 24 hours.

Neurological Outcomes

Table 2 provides a detailed review of the cohort stratified by ASIA grade on admission. At the time of admission, there were 8 ASIA Grade A (24%), 5 Grade B (14%), 8 Grade C (24%), 12 Grade D (35%), and 1 Grade E (3%) patients. Improvement of at least 1 ASIA grade was observed in 19 patients (56%); the remaining 15 patients had the same ASIA grade at admission and discharge. Two patients died during the course of their treatment, resulting in a mortality rate of 6%. One patient suffered from pulseless electrical activity in the field and was resuscitated, but never recovered from other injuries. He was treated aggressively but his Glasgow Coma Scale score never improved above 5T, and the family elected to withdraw care in the context of multiple organ failure. The second death occurred in an elderly patient who fell while standing. The patient developed significant multisystem organ failure that required mechanical ventilation and acute renal replacement therapy. The patient also required reversal of

TABLE 2. Incidence of results stratified by initial ASIA grade*

Variable	ASIA Grade				
	A (n = 8)	B (n = 5)	C (n = 8)	D (n = 12)	E (n = 1)
1-grade improvement	0 (0)	2 (40)	6 (75)	5 (41.67)	0 (0)
2-grade improvement	2 (25)	2 (40)	1 (12.5)	0 (0)	0 (0)
3-grade improvement	1 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)
No improvement	5 (62.5)	1 (20)	1 (12.5)	7 (58.33)	1 (100)
Dopamine administered	8 (100)	5 (100)	6 (75)	11 (91.67)	1 (100)
Phenylephrine administered	5 (62.5)	4 (80)	4 (50)	9 (75)	0 (0)
Dopamine administered first	6 (75)	4 (80)	6 (75)	10 (83.33)	1 (100)
Phenylephrine administered first	2 (25)	1 (20)	2 (25)	2 (16.67)	1 (100)
Dopamine complications	5/8 (62.5)	4/5 (80)	4/6 (66.67)	7/11 (63.64)	1/1 (100)
Phenylephrine complications	4/5 (80)	2/4 (50)	2/4 (50)	2/9 (22.22)	0/0 (0)
Pneumonia	3 (37.5)	2 (40)	1 (12.5)	0 (0)	0 (0)
Respiratory failure	8 (100)	4 (80)	1 (12.5)	2 (16.67)	0 (0)
Urinary tract infection	3 (37.5)	2 (40)	2 (25)	1 (8.33)	0 (0)
Tracheostomy	3 (37.5)	0 (0)	0 (0)	0 (0)	0 (0)
Gastrostomy	1 (12.5)	0 (0)	0 (0)	1 (8.33)	0 (0)
Steroids administered	5 (62.5)	1 (20)	5 (57.5)	9 (75)	0 (0)
No steroids	3 (37.5)	4 (80)	3 (37.5)	3 (25)	1 (100)
Surgery in <24 hrs	4 (50)	3 (60)	3 (37.5)	5 (41.66)	1 (100)
Surgery in >24 hrs	3 (37.5)	2 (40)	3 (37.5)	2 (16.66)	0 (0)
No surgery	1 (12.5)	0 (0)	2 (25)	5 (41.66)	0 (0)
Mean age (yrs)	63.88 ± 15.64	64.40 ± 15.19	63.125 ± 18.11	60.33 ± 15.80	30 ± 0
Mean MAP goals >85 (hrs)	103.5 ± 43.94	149.5 ± 12.37	86.29 ± 51.93	93.583 ± 49.94	72 ± 0
Average ICU LOS (days)	26 ± 22.25	12.8 ± 6.05	6.5 ± 5.10	5.75 ± 2.70	4 ± 0
Average hospital LOS (days)	33.88 ± 25.83	28.6 ± 20.99	12.5 ± 10.80	9.66 ± 9.28	4 ± 0

* Continuous variables are reported as the mean ± SD; categorical data are reported as number (%).

preinjury coagulopathy and suffered from multiple nosocomial infections, which ultimately resulted in his death.

Vasopressor Administration

The characteristics of vasopressor utilization can be found in Table 3. Vasopressors were administered to obtain MAP goals > 85 mm Hg in all patients, for a mean 101 ± 48 hours (4.2 days), before being relaxed to lower goals. This mean time was affected by 2 patients who were transferred to another acute care center for management directly from the ICU while still receiving MAP goals early in their hospitalization. Eighteen patients (53%) had their vasopressor changed due to complications, and 12 patients were concurrently administered 2 or more vasopressors (35%). Dopamine was administered to 31 patients (91%) for MAP

goals, and phenylephrine was administered to 22 patients (65%). A detailed delineation of the vasopressor-associated complications can be found in Table 4. For the entire cohort, there was a nonsignificant trend toward a higher complication rate with dopamine (68% of patients who received dopamine experienced complications [21 of 31 patients] vs 45% for phenylephrine [10 of 22 patients]; OR with dopamine 2.52 [95% CI 0.82–7.78], $p = 0.105$). In the subgroup of patients age > 55 years, dopamine produced statistically significant increases in complications rates when compared with phenylephrine (see Table 5). This effect was not observed in a comparison of dopamine to phenylephrine in the group < 55 years. Further analysis showed that age > 55 years was also associated with all vasopressor complications (90% of older patients experienced complications [18 of 20 patients] vs 52% of younger patients [8 of 14 patients]; OR for older 6.75 [95% CI 1.1–41.00], $p = 0.026$), despite there being no significant differences in injury severity score, mean ASIA improvement, steroid administration, or length of stay, as shown in Table 6. Together these results suggest that dopamine is associated with a higher risk of complications than phenylephrine in older patients.

Complications

Twenty-nine patients experienced at least 1 complication. Table 7 summarizes the complication rates. The most

TABLE 3. Vasopressor utilization (n = 34)

Administration Pattern	No. of Patients (%)
Dopamine administered	31 (91.18)
Phenylephrine administered	22 (64.71)
Dopamine administered first	27 (79.42)
Phenylephrine administered first	7 (20.59)
Patients had 2 vasopressors	18 (52.94)
Patients had 2 or more concurrently	12 (35.29)

TABLE 4. Specific complication rates by individual vasopressor

Complication	No. of Patients (%) [*]	
	Dopamine	Phenylephrine
Patients w/ complications	21 (67.74)	10 (45.45)
Patients w/ multiple complications	2 (6.45)	1 (4.54)
Atrial fibrillation	5 (16.13)	0 (0)
Tachycardia (HR >130 bpm)	9 (29.03)	3 (13.64)
Bradycardia (HR <50 bpm)	4 (12.90)	7 (31.82)
Ventricular tachycardia	3 (9.68)	0 (0)
Troponin levels	2 (6.45)	1 (4.54)

HR = heart rate.

^{*} Percentages are based on the number of patients per category.

common complications were cardiogenic complications associated with vasopressor administration that occurred in 26 patients (76%). Four patients (12%) experienced respiratory failure during the acute phase of their injury. An additional 10 (29%) patients experienced respiratory failure as a complication during the course of their hospitalization. Eight patients (24%) developed urinary tract infections, and 6 patients (18%) developed pneumonia. Five patients (15%) also presented with a concurrent traumatic brain injury. Additional complications and comorbidities included 1 pulmonary embolism without deep vein thrombosis, 1 pneumothorax from central line placement, 1 venous catheter infection, and 1 forehead hematoma and evacuation. No surgical site infections, deep vein thromboses, or strokes were noted.

Discussion

The reviewed cohort of ATCCS patients had cardiogenic complication rates comparable to other studies of vasopressor use in patients with SCI, although our patients received MAP goal support for less than the Level III recommendation of 7 days.^{12,17} Given the retrospective nature of this study, it is difficult to determine if the inability to meet MAP goals was triggered by early termination due to complications or provider discretion. Of note, the mean duration of MAP goals was determined to be approximately 4.2 days, as compared with 7 days proposed for SCI patients by Vale et al.²¹ While limited by the retrospective nature of this study, we believe that this shorter duration is reflective of the treating surgeon's desire to reduce the morbidity of vasopressor use, particularly after surgical decompression.

Similar to the findings in other recent studies that evaluate vasopressor-related complications for trauma and shock, dopamine was the most common first-line vasopressor administered and associated with a higher risk

of complication when compared with phenylephrine.^{6,7} Although phenylephrine was associated with lower complication rates, it is not recommended for use in cervical injury due to its risk of inducing bradycardia.⁴ Despite these recommendations, we noted that almost half of the patients received treatment with phenylephrine, most commonly as a second-line treatment following complications with dopamine. Given the propensity for cardiovascular complications following SCI, including hypotensive neurogenic shock and autonomic dysreflexia-induced hypertension, optimizing vasopressor support is a critically important issue.^{20,27} Considering the high prevalence of ATCCS in elderly patients and our findings of increased risk of dopamine-related complications in elderly patients with ATCCS, further research is needed to determine the optimal MAP guidelines for ATCCS.¹⁴ Since ATCCS is generally a less severe injury than other forms of acute traumatic SCI, caution is warranted when determining supportive interventions, and further research is needed to elucidate the best interventions for this patient population. Our data suggest that any physician administering dopamine in the context of ATCCS, especially for patients older than 55 years, must consider the high complication rates associated with dopamine.

An understanding of vasopressor management protocols for patients with ATCCS will gain even more importance if early data on optimized spinal cord perfusion leads to improved outcomes. Werndle et al. recently reported on a prospective trial, in which intraspinal pressure (ISP) monitors were placed in patients with traumatic SCI.²² These monitors were used to observe the spinal cord perfusion pressure (SCPP) in 18 patients without any complications such as wound infections or cerebrospinal fluid leaks. Their data directly show that elevated MAP due to vasopressor augmentation does result in a direct increase in ISP and SCPP. Studies in animal models of SCI show that microvascular damage and hypoperfusion is associated with increased degeneration after SCI.^{8,11,23} Advanced studies with accurate monitoring via surgically implanted ISP monitors in concordance with neurological improvement scores could contribute to a better understanding of optimal MAP goals in ATCCS patients and provide clear protocols on the issue.

Other Interventions

Our patient population was treated with decompressive surgical intervention at a higher rate and with increased urgency when compared with the published rates in ATCCS and SCI.^{1,19} In our cohort we found that 64% of surgical patients (15 of 26 patients) underwent decompression within 24 hours. Conversely, a study examining patients from a similar time period by Aarabi et al. indicated

TABLE 5. Dopamine- vs phenylephrine-induced complications by age^{*}

Cohort	Dopamine Complications	Phenylephrine Complications	OR (95% CI)	p Value
Entire cohort	21/31 (67.74)	10/22 (45.45)	2.520 (0.816–7.782)	0.105
Age >55 yrs	15/18 (83.33)	7/14 (50)	5.000 (0.987–25.341)	0.044
Age <55 yrs	6/13 (46.15)	3/8 (37.5)	0.700 (0.116–4.232)	0.697

^{*} Value in boldface is statistically significant.

TABLE 6. Comparison of vasopressor complications by age (age > 55 vs < 55 years)*

Variable	Age >55 (n = 20)	Age <55 (n = 14)	OR (95% CI) (when applicable)	p Value
Mean age (yrs)	72.55 ± 10.875	45.79 ± 7.7073		<0.01
Mean ISS	23.73 ± 18.642	23.21 ± 17.564		0.936
Mean MAP goals (hrs)	104.83 ± 52.922	95.57 ± 40.929		0.593
Mean ASIA grade improvement	0.65 ± 0.671	0.93 ± 0.997		0.336
Steroids administered	13 (65.0)	7 (50.0)	1.857 (0.461–7.482)	0.382
ICU LOS (days)	11.70 ± 11.965	11.64 ± 16.402		0.991
Hospital LOS (days)	16.80 ± 15.946	21.29 ± 23.262		0.538
Dopamine administered	18 (90.0)	13 (92.9)	0.692 (0.057–8.470)	0.773
Dopamine complication	15 (83.3)	6 (46.15)	5.833 (1.119–30.403)	0.029
Phenylephrine administered	14 (70.0)	8 (57.1)	1.750 (0.420–7.288)	0.44
Phenylephrine complication	7 (50.0)	3 (37.5)	1.667 (0.283–9.822)	0.571
Any vasopressor complication	18 (90.0)	8 (57.1)	6.750 (1.111–41.001)	0.026

* Continuous variables are reported as the mean ± SD; categorical variables are reported as number (%). Values in boldface are statistically significant.

that 21% (9 of 42) of their patients with ATCCS underwent rapid surgical decompression within 24 hours.¹ This was consistent with another retrospective study where 24% of ATCCS patients (16 of 67) who underwent decompressive surgery were treated within 24 hours.¹⁹ Ultimately, the decision to perform surgery and the timing of surgery were dependent on the treating surgeon. Given the recent results of the Surgical Timing for Traumatic Cervical Spinal Cord Injury Study (STASCIS), which indicated the benefits of early decompression, we found this difference to be significant and noteworthy.⁹ Steroids did not appear to have an impact on the study as the complication rates did not vary between the steroid and nonsteroid groups. The sample size of this study and the lack of significant differences in outcomes and complications between the patients who received steroids and those who did not make it difficult to draw any meaningful conclusions regarding steroids in this population.

Limitations

The primary limitations of this study were the retrospective nature and small sample size of our population. In addition, this retrospective analysis was limited to the course of acute recovery, and neurological outcomes in long-term follow-up may have provided additional insight into the effect of vasopressors. The small sample size is

reflective of the limited number of central cord injuries seen at an individual institution. This limitation may have prevented several associations from reaching significance with $p \leq 0.05$, as many associations approached this statistical cutoff. At our institution, we have adhered to protocol-based management as strictly as possible for several years. As such, nearly all of our patients with acute SCI, including ATCCS, were managed with vasopressors and MAP goals. Though we believe that this practice improves the quality of the care that we provide to patients, the downside is that this has resulted in the lack of a control group for this study. Finally, quantification of ATCCS severity was performed utilizing the ASIA grading system, and this has limitations given the asymmetrical involvement of the upper extremities associated with ATCCS.

Conclusions

Our results provide compelling data concerning vasopressor-associated complication rates in patients with central cord syndrome. We observed a complication rate of 85% for ATCCS injuries, with 76% of patients experiencing cardiogenic complications associated with vasopressor administration. As the US population continues to age, we anticipate a rise in this condition given its increased incidence in the elderly. Based on the results of our analysis, careful consideration of the risks should be made before administering dopamine in the context of ATCCS in patients over 55 years.

Establishing clear MAP guidelines for ATCCS, in addition to SCI in general, is extremely important and warrants thorough investigation. Ideally, we encourage a multicenter prospective study to elucidate the risk-benefit ratio for SCI with a subanalysis of central cord patients. Given the difficulty of establishing this type of protocol, a more rapid and financially obtainable solution may be to conduct a large, multicenter, retrospective review of SCI patients receiving vasopressors in order to compare cross-institutional outcomes and complications while also providing the statistical power to make more confident as-

TABLE 7. Complication rate (n = 34)

Complication	No. of Patients (%)
Pneumonia	6 (17.65)
Respiratory failure on arrival	4 (11.76)
Respiratory failure in hospital	10 (29.41)
Urinary tract infection	8 (23.53)
Tracheostomy	3 (8.82)
Gastrostomy	2 (5.88)
Cardiogenic	26 (76.47)
Complication of any kind	29 (85.29)

assessments of MAP goals. A subgroup analysis of central cord injuries in this type of study would also be extremely valuable for elucidating additional knowledge regarding ATCCS.

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Author Contributions

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Supplemental Information

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The Brain and Spinal Injury Center score: a novel, simple, and reproducible method for assessing the severity of acute cervical spinal cord injury with axial T2-weighted MRI findings

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OBJECT Previous studies that have evaluated the prognostic value of abnormal changes in signals on T2-weighted MRI scans of an injured spinal cord have focused on the longitudinal extent of this signal abnormality in the sagittal plane. Although the transverse extent of injury and the degree of spared spinal cord white matter have been shown to be important for predicting outcomes in preclinical animal models of spinal cord injury (SCI), surprisingly little is known about the prognostic value of altered T2 relaxivity in humans in the axial plane.

METHODS The authors undertook a retrospective chart review of 60 patients who met the inclusion criteria of this study and presented to the authors' Level I trauma center with an acute blunt traumatic cervical SCI. Within 48 hours of admission, all patients underwent MRI examination, which included axial and sagittal T2 images. Neurological symptoms, evaluated with the grades according to the American Spinal Injury Association (ASIA) Impairment Scale (AIS), at the time of admission and at hospital discharge were correlated with MRI findings. Five distinct patterns of intramedullary spinal cord T2 signal abnormality were defined in the axial plane at the injury epicenter. These patterns were assigned ordinal values ranging from 0 to 4, referred to as the Brain and Spinal Injury Center (BASIC) scores, which encompassed the spectrum of SCI severity.

RESULTS The BASIC score strongly correlated with neurological symptoms at the time of both hospital admission and discharge. It also distinguished patients initially presenting with complete injury who improved by at least one AIS grade by the time of discharge from those whose injury did not improve. The authors' proposed score was rapid to apply and showed excellent interrater reliability.

CONCLUSIONS The authors describe a novel 5-point ordinal MRI score for classifying acute SCIs on the basis of axial T2-weighted imaging. The proposed BASIC score stratifies the SCIs according to the extent of transverse T2 signal abnormality during the acute phase of the injury. The new score improves on current MRI-based prognostic descriptions for SCI by reflecting functionally and anatomically significant patterns of intramedullary T2 signal abnormality in the axial plane.

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KEY WORDS spinal cord injury; MRI; T2; ASIA; contusion; BASIC; trauma

ABBREVIATIONS AIS = American Spinal Injury Association (ASIA) Impairment Scale; BASIC = Brain and Spinal Injury Center; PACS = picture archiving and communication system; SCI = spinal cord injury.

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FOLLOWING the advent and widespread implementation of MRI in the 1980s, many researchers have investigated the prognostic value of MRI findings in assessing acute spinal cord injury (SCI). In particular, the prognostic value of abnormalities in T2-weighted MRI signals has been extensively explored.^{3,4,10,13,15,19,27,30,32,42} In the acute phase, a T2 signal abnormality within the injured spinal cord has been attributed to various underlying pathological changes in both human and animal studies.^{8,25,26,31} For example, a T2 hypointense signal reflects the susceptibility-related T2-shortening effect of intracellular deoxyhemoglobin during the acute and subacute phases of hemorrhage.¹⁴ A T2 hyperintense signal is less specific and probably reflects a combination of vasogenic edema, cytotoxic edema, axonolysis, myelinolysis, inflammatory cellular infiltrate, and petechial hemorrhage.^{25,28,31} Early MRI-based classification systems for acute SCIs defined 3 distinct patterns of intramedullary signal change: Type I, with diffuse T2 hypointensity; Type II, with intramedullary T2 hyperintensity; and Type III, with central T2 hypointensity and a surrounding hyperintense signal.^{3,10,20} Modification of these descriptions in subsequent studies eliminated the Type I pattern because a T2 hypointense hemorrhage was not routinely observed without a significant surrounding T2 hyperintense edema.^{12,33}

A more widely adopted classification system defines 4 distinct injury patterns as assessed on a sagittal T2-weighted MRI sequence.^{1,4,23,33,35} Pattern 1 represents a normal spinal cord signal; Pattern 2 shows a T2 hyperintense intramedullary edema, with its longitudinal extent confined to a single vertebral level; Pattern 3 indicates a multilevel edema; and Pattern 4 includes a mixed hemorrhage and edema.⁴ Such classification systems have been shown to provide measures that correlate with injury severity and that supplement other clinical measures for predicting clinical outcome.^{1,11,12,23,32,35}

Patterns based on sagittal T2-weighted MRI signals are most accurate at predicting outcomes when patients have very mild (that is, Pattern 1, indicating a normal cord signal) or severe (Pattern 4, with hemorrhage and edema) injury.⁴ However, in the setting of nonhemorrhagic intramedullary T2 hyperintensity, there is tremendous variability in clinical outcomes. For example, in a meta-analysis, Bozzo et al. reported that among 49 patients presenting with Pattern 3 edema (that is, with multilevel T2 hyperintensity), the injury severity grades of the American Spinal Injury Association (ASIA) Impairment Scale (AIS) were nearly equally distributed at the follow-up: 27% of these patients had an AIS grade of A, 22% of B, 24% of C, and 24% of D.⁴ This wide variability in outcome data is in part related to the arbitrary measurement of the longitudinal extent of the T2 signal relative to the height of the vertebral body, in addition to the nonspecific nature of T2 hyperintensity in the spinal cord. Histopathological studies of SCI in animals have revealed that longitudinal measurements do not correlate with functional recovery as well as axial or cross-sectional area does.⁵ In addition, translational studies of axial T2 images in rats have indicated a strong correspondence of axial MRI findings with microscopic histopathology and functional recovery.²⁸

Given the limitations of previous longitudinal MRI-

based measures of intramedullary signal change and the paucity of axial T2 data on SCIs, we sought to develop a simple and reproducible classification system for blunt traumatic SCI that is based on the transverse extent of intramedullary T2-weighted MRI signal abnormality during the acute phase of injury. We hypothesized that such a classification system would reflect the functionally relevant anatomical distribution of pathological MRI signal changes and therefore yield valuable diagnostic and prognostic information. In this study, we aimed to assess the reliability and validity of this MRI-based classification system in a cohort of patients with blunt traumatic SCIs.

Methods

Patient Selection

We performed a retrospective chart review to evaluate the diagnostic and prognostic values of axial T2-weighted MRI findings for rating the severity of acute SCIs in patients admitted to San Francisco General Hospital, a Level I trauma center, between January 2005 and December 2011. This study was approved by the internal review board of the University of California. Patients' records were reviewed in a Department of Neurosurgery database and in cross-referencing trauma logs, with searchable terms and by using electronic medical records (San Francisco, CA). From this database, we retrospectively identified the records of 131 patients who had a principal diagnosis of SCI (codes 953–957 designating discharge diagnoses) according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Of these patients, 92 had cervical levels of injury, 60 of whom met this study's inclusion criteria.

To be eligible for this study, patients had to be 18 years of age or older; had to have an MRI examination performed within 48 hours of admission which, at a minimum, included T2-weighted images of the cervical spine in both the axial and sagittal planes; and had to have a documented AIS grading performed both at the time of admission and at a follow-up (performed at the time of discharge from the acute-care hospital). We excluded patients younger than 18 years; those with an SCI related to penetrating trauma or with imaging evidence of complete spinal cord transection; and those with MRI studies degraded by motion or other artifacts such that T2-weighted images were nondiagnostic as assessed by a neuroradiologist (J.F.T.). Patients who underwent surgical decompression, fusion, or both before the MRI examination were also excluded. SCI-trained physiatrists and neurosurgical and neurocritical care attending physicians performed the AIS grading. All eligible patients' AIS grades were obtained within 24 hours of admission and before the MRI examination.

MRI Studies

All MRI studies were performed on a 1.5 T GE Genesis Signa scanner (GE Healthcare). Axial T2-weighted fast spin echo imaging was performed with the following parameters (means \pm SDs from 10 randomly selected examinations): TR 3590 \pm 546 msec, TE 94.9 \pm 10 msec, slice thickness 3 mm, and echo train length 16 \pm 4. Sagittal T2-weighted fast spin echo imaging was performed

with the following parameters: TR 3300 ± 290 msec, TE 102 ± 3 msec, slice thickness 3 mm, and echo train length 15 ± 3 . For both sagittal and axial T2 imaging, the acquisition matrix was 256×256 . The phase encoding direction was left to right for the axial sequences and craniocaudal for the sagittal sequences. The field of view ranged from 16 to 20 cm. Additional sequences performed as part of our routine trauma MRI protocol were not evaluated for the purposes of this study. An axial 2D multiecho recombined gradient echo sequence from a single normal patient was used as a control reference for identifying margins of gray matter at the upper, mid, and lower cervical levels.

Image Analysis and BASIC Scoring

Axial and sagittal T2-weighted MRI sequences were examined by a fellowship-trained neuroradiologist (J.F.T.) and a spine fellowship-trained neurosurgeon (S.S.D.), who were both blinded to the AIS grade. The epicenter of the SCI was located on the axial T2-weighted sequence and confirmed by cross-referencing with the sagittal T2-weighted sequence. A single axial image with the most severe SCI was identified for the scoring. The Brain and Spinal Injury Center (BASIC) scoring was performed according to the observations outlined in Fig. 1. Briefly, an SCI with a BASIC score of 0 represented normal spinal cord T2 relaxivity without appreciable pathological intramedullary signal. A BASIC score of 1 represented cases in which a pathological T2 hyperintensity was approximately confined to the spinal gray matter (Fig. 2). A BASIC score of 2 was assigned when a pathological intramedullary T2 hyperintensity extended beyond the margins of the central gray matter and obscured the gray-white margins, but

did not involve the entire transverse extent of the spinal cord. For these cases, some peripheral normal-appearing white matter was identified. A BASIC score of 3 was assigned when the pathological T2 hyperintensity involved the entire transverse extent of the spinal cord, without any residual normal-appearing white matter. An SCI with a BASIC score of 4 was defined as a BASIC Score 3 injury with additional superimposed discrete foci of intramedullary T2 hypointensity attributed to the presence of macroscopic intramedullary hemorrhage.

The SCIs with BASIC scores of 0, 1, and 2 could be elevated by a single score if a macroscopic hemorrhage was present, although no such cases were identified in our patient cohort. For example, a BASIC score of 2 with the presence of macroscopic hemorrhage would be elevated to BASIC score of 3.

Image Processing

Digital Imaging and Communications in Medicine (DICOM) images from our university picture archiving and communication system (PACS; Agfa Healthcare) were annotated and cropped for figure production with ImageJ software (available at <http://rsb.info.nih.gov/ij> and developed by Wayne Rasband at NIH). We produced 3D-color surface plots of T2-weighted images with an interactive 3D-surface plot plugin for ImageJ. These surface plots were used only for figure production and were not used for primary image analysis or interrater reliability testing.

Interrater Reliability Testing Protocol

Interrater reliability was assessed by measuring the mean and SD of scores assigned by multiple raters review-

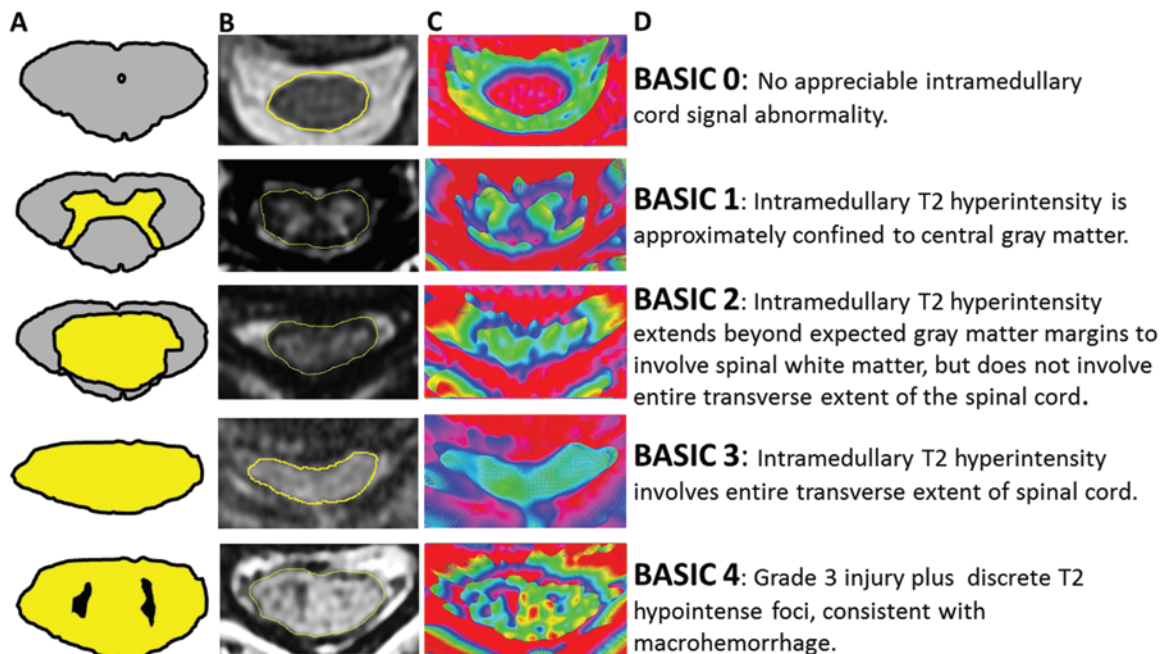


FIG. 1. The BASIC score of SCIs. Cartoon schematics (A), representative axial T2-weighted MRI scans (B), 3D-color surface plots based on the axial T2 image (C), and brief definitions (D) for each of the 5 BASIC scores (ranging from 0 to 4). In the representative MRI scans (B), the external contour of the spinal cord is outlined in yellow for better delineation. Figure is available in color online only.

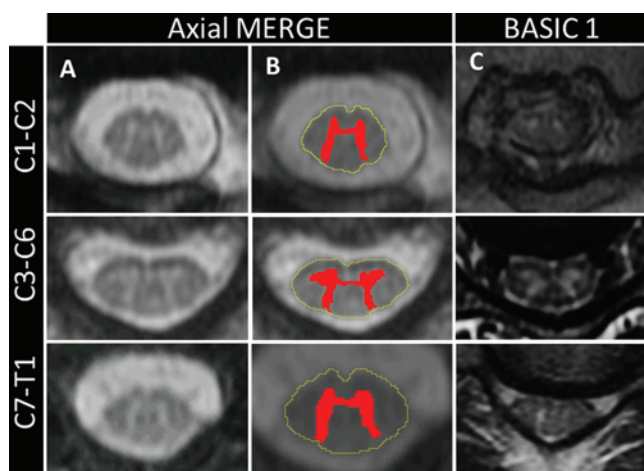


FIG. 2. Familiarity with the normal spinal cord gray matter morphology at rostral (C1–C2), middle (C3–C6), and caudal (C7–T1) cervical vertebral levels is important for rating an SCI as BASIC Score 1. **A:** Axial multi-echo recombined gradient echo (MERGE) image of the normal spinal cord clearly indicates the normal gray matter morphology at the upper, middle, and lower cervical vertebral levels. **B:** Manual segmentation of cervical spinal cord gray matter based on an axial MERGE images in A with the peripheral cord contour delineated in yellow. Note the large frontal horns related to the cervical enlargement at the C3–6 vertebral levels. **C:** Axial T2-weighted images from the epicenters of BASIC Score 1 SCIs at the upper, middle, and lower cervical vertebral levels. Note that the T2 hyperintensity represents the approximate boundaries of spinal cord gray matter for each cervical level. Figure is available in color online only.

ing 20 MRI studies chosen to represent all parts of the BASIC rating scale; the reliability testing was similar to that in the development of the scale established by Basso, Beattie, and Bresnahan.² Seven participating raters were instructed in the rating during an initial training session in which they were shown MRI studies of a range of SCIs and the method of scoring was explained. The specialties of training of the participants included neuroradiology, neurosurgery, emergency medicine, neuroanatomy, and anesthesiology. The rating of individual images was then practiced in concurrent discussions, followed by each participant silently rating the observations on the MRI studies and then comparing and discussing their scores with those of the instructors.

After the training, each rater was presented with a series of DICOM images including both the injury epicenter and adjacent normal-appearing spinal cord from 20 separate cases from our cohort with SCIs representing all levels of the BASIC scale. The cases were presented in random order. Also provided to each rater were a set of data-recording sheets, an overview of the project background and goals, a set of frequently asked questions with answers, and a score determination guide for ease of assigning scores. All participants then individually examined the 20 images and scored each of them within 20 seconds according to the descriptions provided. The data sheets were then collected, analyzed, and compared with a consensus score for each image, arrived at by the original scale developers' viewing, discussing, and arriving at the consensus score for each image. This consensus score

was determined after all raters (including the experienced raters) had completed and submitted their independent ratings of the images.

Statistical Analysis

All statistical analyses were performed with a commercial software package (SPSS Inc.). Statistical correlation between the BASIC score and AIS grades at both admission and discharge were evaluated with the Pearson correlation coefficient. The differences in BASIC scores among the AIS improvement groups were analyzed with 2-tailed Student t-tests. Statistical significance was determined as $p < 0.05$.

A statistical analysis of the reliability of the BASIC classification system among different observers against the consensus scores was performed with the Kappa coefficient (κ). As described by Landis and Koch,²¹ a κ of > 0.8 was interpreted as excellent reliability. The unidimensional nature of the BASIC score was assessed on all cases by all raters with exploratory factor analysis with the principal component extraction method.^{29,36}

Results

Patient Characteristics

Table 1 shows the demographic and clinical characteristics of our cohort of 60 patients. Table 2 lists the complete admission and discharge AIS data for our entire cohort. All of the SCIs resulted from blunt trauma, and 17 of the patients (28%) presented with complete injury (that is, AIS Grade A). The patients were predominantly male (70%) with a mean age of 56 years (range 18–94 years) (Table 1). The most frequent injury mechanism was fall (53%), followed by motor vehicle collision (15%), bicycle accident (10%), assault (8%), pedestrian versus automobile accident (7%), and other or nonspecified mechanism (7%) (Table 1). The mean length of time between the hospital admission and the spine MRI was 8.6 ± 6 hours (range 1–39 hours). The patients were examined at the sole Level I trauma center within a dense urban catchment area where the time from injury to admission at our institution is on average less than 60 minutes. In total, 51 patients

TABLE 1. Characteristics of the patients in this study

Variable	All Patients
Total no. of patients	60
Mean age in yrs \pm SD (range)	56 ± 20 (18–94)
Sex M/F (%)	42/18 (70/30)
Injury mechanism, no. of patients (%)	
Fall or jump	32 (53)
Motor vehicle collision	9 (15)
Bicycle accident	6 (10)
Assault	5 (8)
Pedestrian vs automobile accident	4 (7)
Other	4 (7)
Time to MRI in hrs \pm SD (range)	8.6 ± 6 (1–39)
Mean time to discharge in days \pm SD	23 ± 24

TABLE 2. The AIS grades of the 60 patients in this study at admission and at discharge

AIS Grade	No. of Patients (%)	
	Admission	Discharge
A	17 (28)	9 (15)
B	7 (12)	4 (7)
C	10 (17)	10 (17)
D	18 (30)	20 (33)
E	8 (13)	17 (28)

(85%) underwent an MRI examination within 12 hours of the hospital admission, and only 1 patient (2%) underwent the examination more than 24 hours after admission. For those patients admitted to the hospital, the average length of hospitalization was 23 days (range 4–128 days).

MRI Findings

Axial and sagittal T2-weighted MRI sequences indicated intramedullary signal abnormalities in 48 (80%) of the 60 patients. In all patients, 5 distinct patterns of intramedullary signal were identified on the axial T2-weighted sequence at the injury epicenter (Fig. 1). In 12 patients (20%), no apparent signal abnormality was observed, and their SCI finding received a BASIC score of 0. In 16 (27%) of the patients, a T2 signal hyperintensity was observed that largely conformed to the expected morphology of the central spinal gray matter; therefore, these patients' SCI was rated as BASIC Score 1. In 18 patients (30%), we observed a pattern of intramedullary T2 hyperintensity at the injury epicenter that extended beyond and obscured the expected margins of the central gray matter, but did not involve the entire transverse extent of the spinal cord on axial imaging; their injuries were therefore rated BASIC Score 2. In 9 patients (15%), an SCI resulting in diffuse intramedullary T2 hyperintensity that involved the transverse extent of the cord was rated as BASIC Score 3. The remaining 5 patients (8%) had SCIs that resulted in diffuse T2 hyperintensity with superimposed discrete foci of T2 hypointensity, consistent with intramedullary hemorrhage, and their SCI severities were rated as BASIC Score 4. None of the patients showed evidence for macroscopic hemorrhage in the absence of diffuse transverse T2 hyperintensity.

BASIC Score Strongly Correlates With Admission AIS Grade

We observed a highly significant correlation between the AIS grade at the time of admission and the morphological pattern of intramedullary signal abnormality as rated by the BASIC score on the admission MRI study. Figure 3 graphically displays the linear correlation between the AIS grade and the BASIC score at admission. Along the severe spectrum of an acute SCI, a BASIC score of 3 or 4 was nearly always associated with an admission AIS grade of A, that is, in 13 (76%) of the 17 patients with an admission AIS Grade A. Among the 43 patients with an AIS grade less severe than A, only 1 patient (2%) had

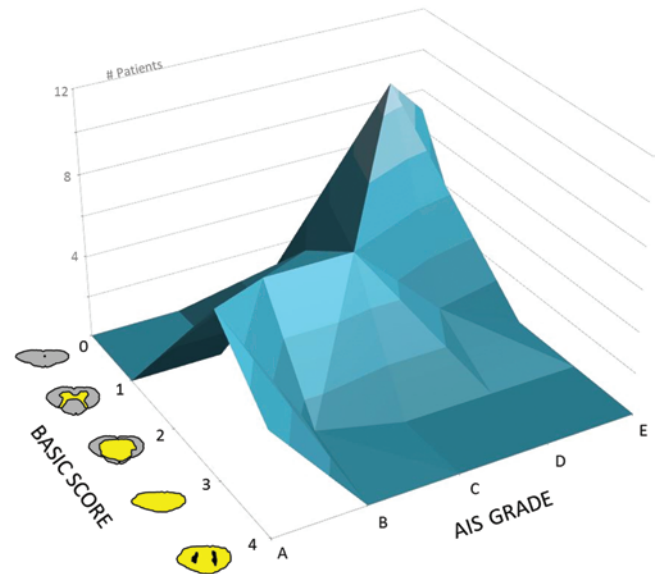


FIG. 3. A 3D surface plot indicates a strong correlation of the BASIC score with the AIS grade at the time of hospital admission (Pearson coefficient = -0.877 , $p = 4.0 \times 10^{-20}$). The height of the surface plot (that is, the z-axis) corresponds to the number of patients with corresponding BASIC scores and AIS grades within our cohort. Note the course of the peak of the surface plot clearly tracing the strong linear correlation between the BASIC score and the AIS grade. Figure is available in color online only.

a BASIC score of 3, and none had a BASIC score of 4. A BASIC score of 4 was always observed with an SCI rated as AIS Grade A at admission. Thus, a high BASIC score, that is, of 3 or 4, was specific for severe injury at admission.

On the mild end of the SCI severity spectrum, an SCI with a BASIC score of 1 or 0 was never observed in patients with an AIS grade of A or B on admission. A BASIC score of 0 (that is, a normal cord signal) was entirely limited to patients with an admission AIS grade of D or E.

BASIC Score Strongly Correlates With AIS Grade at Discharge

The correlation between the AIS grade at the time of discharge and the BASIC score based on the morphological pattern of intramedullary signal abnormality on the admission MRI study was also highly significant. Figure 4 displays the linear correlation between the admission AIS grade at discharge and the BASIC score. Figure 5 shows a plot of the admission and discharge AIS grades for all patients stratified by the 5 BASIC score groups. Of 12 patients with an SCI rated as BASIC Score 0, 11 (92%) were discharged with an AIS Grade E, with the remaining single patient discharged with AIS Grade D. All 16 patients with a BASIC score of 1 were discharged with an AIS grade of D or E. Of 18 patients with a BASIC score of 2, 16 (88%) were discharged with an AIS grade of C or D. Among 9 patients with a BASIC score of 3, 6 (67%) were discharged with an AIS grade of A or B. All 4 patients with a BASIC score of 4 were discharged with an AIS grade of A.

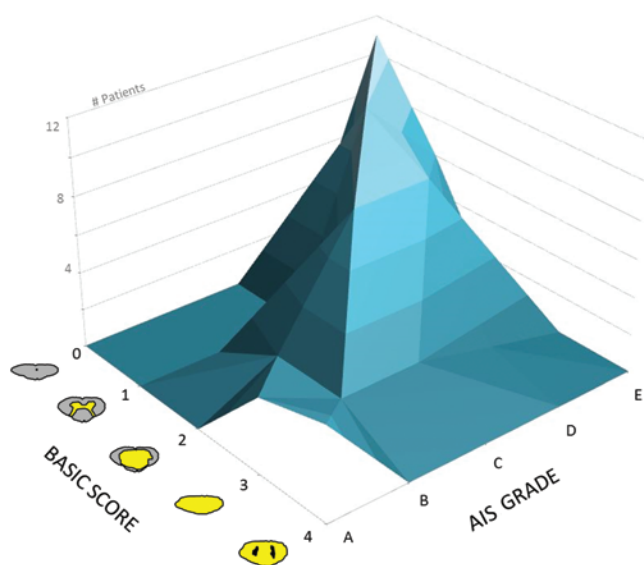


FIG. 4. A 3D surface plot indicates a strong correlation between the BASIC score and the AIS grade at the time of hospital discharge (Pearson coefficient = -0.880 , $p = 2.0 \times 10^{-20}$). The height of the surface plot (that is, the z-axis) corresponds to the number of patients with corresponding BASIC scores and AIS grades within our cohort. Note the course of the peak of the surface plot clearly tracing the strong linear correlation between the BASIC score and the AIS grade. Figure is available in color online only.

BASIC Score Distinguishes Patients With an Admission AIS Grade of A Who Improve at Discharge

At the time of discharge, 8 (47%) of the 17 patients with an admission AIS grade of A improved by at least one AIS grade. The BASIC scores among AIS Grade A patients whose condition did not improve were significantly higher than among those who did improve by at least one AIS grade (3.6 ± 0.5 vs 2.6 ± 0.5 , respectively, $p < 0.01$; Fig. 6).

BASIC Score and Interobserver Reliability

The mean and median κ scores for all raters were 0.83 and 0.81, respectively (both $p < 0.00001$), relative to the consensus score, consistent with excellent reliability and reproducibility. A factor analysis with principal component analysis indicated that the BASIC score represented a unidimensional outcome, with high correspondence among the 7 raters (Table 3 and Fig. 7).

Discussion

In the present study, we sought to classify the severity of an acute SCI according to the transverse extent of signal abnormalities as qualitatively assessed on a single axial T2-weighted MR image centered at the lesion epicenter. Specifically, we introduce a 5-point (ranging from 0 to 4) ordinal classification system, which encompasses the spectrum of SCI severity, from a normal-appearing spinal cord to a diffusely abnormal cord signal hyperintensity with superimposed macroscopic intramedullary hemorrhage (Fig. 1). We excluded cord transection injuries from consideration because of the distinct and easily distinguished imaging pattern associated with this SCI type. The proposed BASIC score builds on previously described MRI-based systems for classifying acute traumatic SCIs, and in our analyses it strongly correlated with AIS grades at the hospital admission for the SCI and at discharge (Figs. 3 and 4). Moreover, the BASIC score stratifies the SCIs on the basis of the anatomically and functionally relevant extent of transverse injury. It may help identify those patients who present with the most severe clinical injury (that is, with AIS Grade A) and who will improve by at least one AIS grade by the time of discharge (Fig. 6).

Both human and animal studies have demonstrated that the transverse extent of an SCI and relative white matter sparing are major determinants of functional outcomes.^{5,6,16,18,22} To our knowledge, the present study is the first to correlate clinical symptoms and outcomes with the

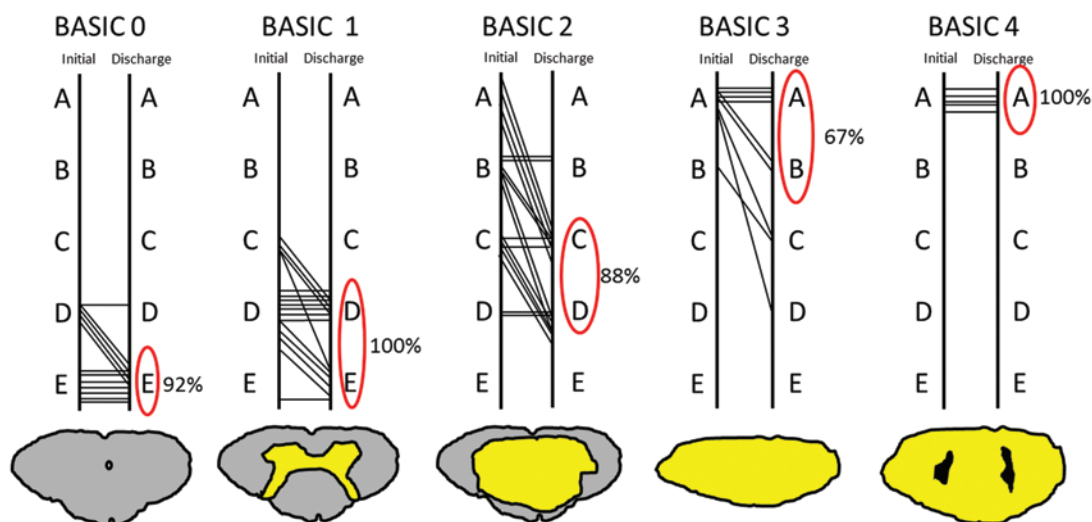


FIG. 5. Admission and discharge AIS grades for all patients in our cohort are plotted within each BASIC score group, with a cartoon schematic of the SCI below each plot. The percentages of patients within each BASIC group with a discharge AIS grade circled in red are listed to the right of the discharge AIS grades. Figure is available in color online only.

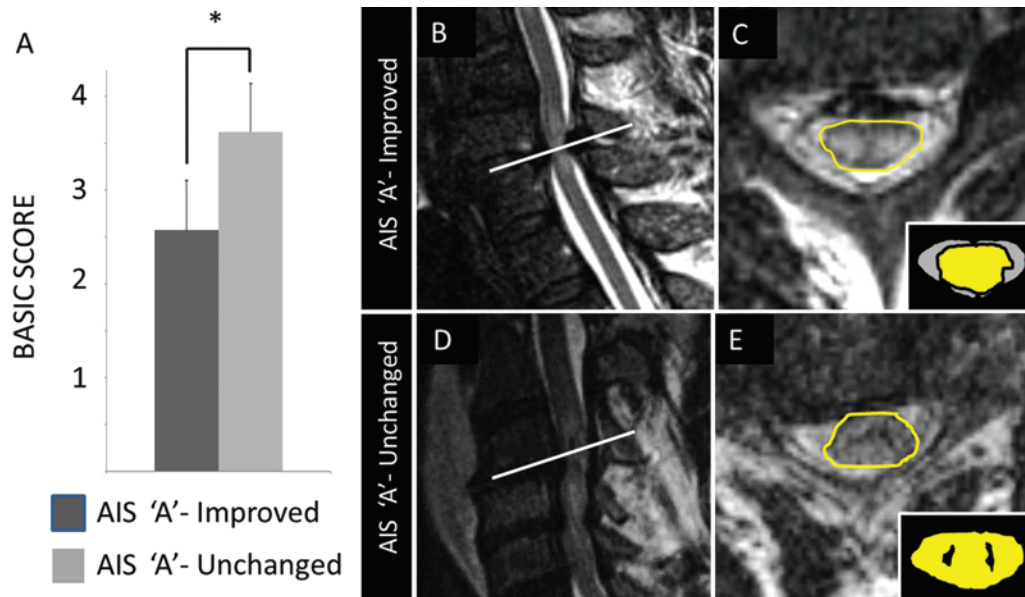


FIG. 6. The BASIC scores for patients who presented with complete injury (that is, with AIS Grade A) and who improved by at least one AIS grade are significantly lower than those for AIS Grade A patients whose SCI showed no improvement. The bar graph shows a significantly lower BASIC score for patients with AIS Grade A whose injury improved in AIS grade by the time of follow-up compared with AIS Grade A patients whose injuries did not improve ($p < 0.01$) (**A**); error bars indicate the SD. Sagittal (**B**) and axial (**C**) T2-weighted images from a patient with an SCI sustained in a fall and presenting with AIS Grade A indicate abnormal intramedullary T2 hyperintensity with a pattern of T2 signal abnormality on the axial image at the injury epicenter (**B**) consistent with a BASIC score of 2 (see schematic **inset** in the right lower corner). This patient's condition improved to AIS Grade C at the follow-up. Sagittal (**D**) and axial (**E**) T2-weighted images from a patient with an SCI injury due to an assault and also presenting with AIS Grade A show abnormal intramedullary T2 signal at the injury epicenter (**D**) consistent with a BASIC score of 4 (see schematic **inset** in the right lower corner). This patient did not recover from the SCI at the time of follow-up. White lines in **B** and **D** approximate the level of the axial T2 image for each patient. For better delineation, the peripheral margins of the spinal cord are outlined in yellow in **C** and **E**. Figure is available in color online only.

transverse extent of MRI T2 signal abnormality in the axial plane in humans. Rather than arbitrary measurements of the longitudinal extent of signal abnormality in the sagittal plane, axial imaging enables the definition of anatomically relevant spinal involvement in a graded manner. With an SCI severity rated as BASIC Score 1, T2 hyperintensity is approximately confined to the spinal gray matter. The relatively good clinical outcomes at discharge for patients with a BASIC score of 1 in our study (all of these patients were discharged with an AIS grade of D or E) suggest such signal abnormality does not reflect significant coagulative necrosis or irreversible frontal horn disruption, but more likely represents vasogenic edema, as has been suggested by other authors.^{9,31}

When a T2 hyperintense signal extended beyond the approximate confines of gray matter (that is, in patients with BASIC scores of 2–4), patients had a worse prognosis (Fig. 5). Importantly, distinguishing patients who have some spared white matter signal (a BASIC score of 2) from those with diffuse transverse T2 hyperintensity (a BASIC score of 3) allows for identifying those patients whose SCIs would all be classified as having multilevel hyperintensity according to previous sagittal T2 signal grading systems.⁴ Our observations of a functionally relevant distinction between SCIs rated as BASIC Score 2 or 3 are consistent with preclinical data, and this corroboration highlights the important role of spared white matter

in predicting outcomes.^{6,17,18,22} In our cohort, patients with a BASIC score of 2 fared better than those with a BASIC score of 3, with 88% of BASIC Score 2 patients achieving an AIS grade of C or D and no AIS Grade A at discharge, as opposed to 67% of BASIC Score 3 patients discharged with AIS Grade A or B (Fig. 5).

Consistent with results based on previous classification systems,^{3,12,24,27} the presence of macroscopic intramedullary hemorrhages in our cohort predicted a poor prognosis. All of the patients with a BASIC score of 4 were

TABLE 3. Principal component analysis of the BASIC score for each rater and the consensus

Rater No.	Principal Component 1
1	0.966
2	0.988
3	0.769
4	0.971
5	0.845
6	0.915
7	0.947
Consensus score*	0.988

* The consensus score of 20 images used for the interrater testing was collaboratively arrived at by the 2 developers of the BASIC score scale.

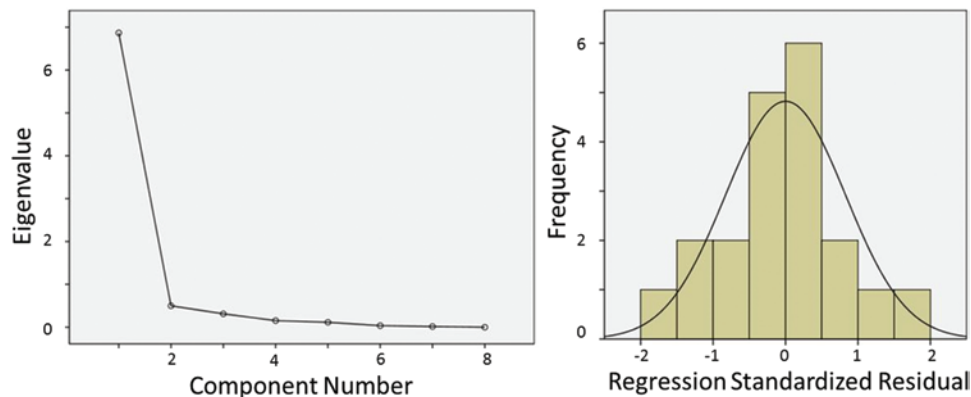


FIG. 7. **Left:** A screen plot of factor analysis (via principal component analysis extraction) on all ratings, indicating that the BASIC scores for SCIs reflect a unidimensional linear metric characterized by a single principal component with an eigenvalue of > 1 . **Right:** A principal-component loading matrix indicating that all raters' scores as well as the consensus score loaded very highly onto the BASIC score unidimensional factor (that is, on Principal Component 1). The frequency of residual errors relative to the consensus scores was normally distributed, indicating that novice ratings, on average, strongly and linearly correlated with the expert consensus rating, with only a small number of normally distributed random errors. Together, these results suggest that the BASIC score has high interrater reliability and good parametric properties (see also Table 3). Figure is available in color online only.

discharged with an unchanged AIS Grade A. Of note, we did not use gradient- or susceptibility-weighted sequences, which have demonstrated increased sensitivity to intramedullary blood products.⁴⁰ Further studies are required to evaluate the prognostic value of these more sensitive susceptibility-weighted sequences. Importantly, not all of the patients presenting with AIS Grade A had evidence of macroscopic hemorrhage or diffuse axial T2 hyperintensity. We observed that some patients who presented clinically with complete injury had BASIC scores that suggested a less severe injury (Fig. 6).

Less severe BASIC scores were more commonly observed in those patients with AIS Grade A SCIs that improved by at least one AIS grade by the time of discharge. Thus, the BASIC score discriminated between AIS Grade A patients at presentation whose condition improved by at least one AIS grade by the time of discharge, and those who showed no improvement as assessed by the AIS grading (Fig. 6). While longer-term follow-up and prospective data are needed to corroborate these preliminary results, the present data suggest that the BASIC score may be very helpful in identifying those patients who are the best candidates for clinical trials of experimental higher-risk invasive procedures such as intramedullary injection of stem cells or devices.

The slightly older demographic of the patients in our cohort differs from the typical demographics reported for patients with acute traumatic SCIs.^{7,34} This shift represents a trend we have observed for all SCIs at our institution, with an older second peak in SCI patients after a fall. This appears to reflect the specific population demographic of the San Francisco Bay area. Similar trends have been recently reported in the Canadian population.³⁹ Although a demographic subgroup analysis was not performed, no notable differences in patterns of transverse intramedullary T2 signal hyperintensity among age group or injury mechanisms were observed. However, to validate the BASIC score, future studies including larger patient populations across geographic regions are warranted.

Limitations

There are limitations to the current study, including its retrospective design, variable timing of the acute-phase MRI, and a relatively short clinical follow-up. In addition, interrater reliability testing was not performed directly at a PACS station but rather in a group setting with presentation of index images selected by a neuroradiologist from the injury epicenter and from normal spinal cord. In our opinion, it is in fact easier to assign a BASIC score by scrolling through the axial and sagittal MRI studies on a dedicated PACS station, as is the typical practice followed by most spine surgeons and radiologists. Prospective validation studies with long-term follow-up are planned to validate these preliminary data. An additional limitation is the subjectivity of our classification system. Although qualitative and subjective in nature, the BASIC score scale demonstrated excellent interrater reliability (mean κ score = 0.83) across observers with varied expertise. Moreover, it can be performed rapidly without performing manual measurements or time-consuming image postprocessing. Axial T2-weighted imaging is routinely performed as part of MRI protocols for cervical spine trauma and as a recommended sequence for acute spinal cord MRI protocols according to the SCI Common Data Elements of the National Institute of Neurological Disorders and Stroke (NINDS). Therefore, a modification of existing protocols is not required. One limitation of T2 signal-based MRI classification systems such as BASIC for SCI evaluation is the nonspecific nature of the T2 signal hyperintensity. This probably contributes, at least in part, to some of the variable clinical outcomes we observed in patients within each BASIC score group (Fig. 5).

Changes in T2 signals also depend on the timing of the MRI after an injury.^{23,26,28,38} Although we excluded all patients who underwent an MRI examination more than 48 hours after admission and even though 85% of our patients had MRI within 12 hours of admission, the variable timing of the MRI examination within our selected time interval

also probably influenced the patterns of observed T2 signal abnormality in the setting of a rapidly evolving acute SCI. Further studies evaluating the optimal timing of MRI examinations for prognostic purposes during the acute phase of SCI are needed. Despite these limitations and when compared with previous classification systems^{3,4,12,35} on which it is built, the BASIC score has excellent prognostic capability, particularly for patients with intermediate injury severity. Advanced MRI techniques, including diffusion tensor imaging, magnetization transfer imaging, MR spectroscopy, and functional MRI have shown varying potentials as noninvasive functional biomarkers for SCI.^{37,41} The prognostic superiority of these techniques to standard T2-weighted imaging will need to be established before their routine clinical implementation. The BASIC score for SCIs may represent one standard for such future comparisons.

Conclusions

We present a novel, simple, and reliable classification system for grading acute blunt traumatic SCIs on the basis of the pattern of T2 signal abnormality as assessed in the axial plane at the injury epicenter. The BASIC scale has excellent prognostic potential across all SCI severities. These preliminary data suggest that the BASIC score will help distinguish patients who present with an AIS Grade A that improves before discharge from those who will not recover significant function. The proposed classification system builds on the previous literature and may provide prognostic stratification of patients with SCIs by reflecting functionally and anatomically significant patterns of T2 hyperintensity in the axial plane, which is not dependent on arbitrary measures of longitudinal signal abnormality. Future prospective and well-controlled studies are needed to further validate the prognostic value of the BASIC score.

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Author Contributions

Conception and design: Dhall, Talbott. Acquisition of data: Dhall, Talbott, Whetstone, Readdy. Analysis and interpretation of data: Dhall, Readdy, Mabray. Drafting the article: Talbott. Critically revising the article: Dhall, Whetstone, Ferguson, Bresnahan, Beattie, Pan, Manley. Reviewed submitted version of manuscript: Bresnahan, Beattie, Pan, Manley, Saigal, Hawryluk. Statistical analysis: Ferguson. Study supervision: Dhall.

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SPINAL CORD INJURY REDCAP DATABASE

Redcap Data Dictionary

Total Variables Collected

As of 10/05/2015: 1,294 Variables

NINDS Common Data Element (CDE) Count

Core-CDE: 199 Variables

Supplementary-CDE: 642 Variables

Exploratory-CDE: 43 Variables

Patient Demographics

General Demographics

Study ID

Medical Record Number

(S-CDE) Facility Name

Patient Last Name

Patient First Name

Year of Injury

(S-CDE) Patient Age at Time of Injury

(C-CDE) Birth Date

(C-CDE) Patient Gender

(C-CDE) Date of Injury

(C-CDE) Time of Injury

Time of Injury Above is

Admitted Service

Primary Insurance Code

Primary Insurance Name

Secondary Insurance Code

Secondary Insurance Name

(C-CDE) Race

(C-CDE) Ethnicity

Language Spoken

(C-CDE) Number of Years of Education

(S-CDE) Marital/Partner Status

(S-CDE) Number of Members in Patient's Household (Including Patient)

(S-CDE) Area of Residence

(S-CDE) Primary Occupation

(S-CDE) If indicated Other for previous question, please specify.

(S-CDE) If indicated Paid Work for previous question, please specify.

(S-CDE) Secondary Occupation

(S-CDE) If indicated Other for previous question, please specify.

(S-CDE) If indicated Paid Work for previous question, please specify.

(S-CDE) Family Income Range

(E-CDE) How do you get along with your current household income?

(S-CDE) Birth Country Name

(E-CDE) Citizen of USA

Deceased Status

(S-CDE) Patient is Deceased?

Patient Deceased While At Hospital

(S-CDE) Date of Death
(S-CDE) Time of Death
(S-CDE) Primary Cause of Death
(S-CDE) Secondary Cause(s) of Death

Consent and Contact Information

Study Consent

Initial Consent Status
Initial Consent Date
If patient initially enrolled and given blood draw under "Waiver of Consent", Surrogate has signed off to enroll the patient.
Surrogate Full Name
Surrogate Home Phone Number
Surrogate Cell/Alternate Phone Number
Surrogate Address
Surrogate Email Address
Surrogate Relationship to Patient
Subject Reconsent (for patients initially enrolled via waiver or surrogate consent)

Patient Contact Information

Patient Address
Patient Email
Patient Home Phone Number
Patient Cell/Alternate Phone Number
Name of Primary Contact
Phone Number of Primary Contact
Primary Contact's Relationship with Patient

Other Spinal Cord Injury Studies

Enrolled in Other SCI Studies/Trials?

Biospecimens Collection

24 Hour Blood Draw

24 Hour Blood - Was Blood Drawn?
24 Hour Blood - Draw Time
24 Hour Blood - Processing Time
24 Hour Blood - Freezer Time
24 Hour Blood - Notes

48 Hour Blood Draw

48 Hour Blood - Was Blood Drawn?
48 Hour Blood - Draw Time
48 Hour Blood - Processing Time
48 Hour Blood - Freezer Time
48 Hour Blood - Notes

Medical History

Prior Medical History

(S-CDE) Date Medical History Taken
(S-CDE) Does the participant have a history of any medical problems/conditions in the following body systems?
(C-CDE) Please describe allergic/immunologic history indicated above. Include start/end date.

(S-CDE) Is allergic/immunologic condition described above ongoing?

(C-CDE) Please describe cardiovascular history indicated above. Include start/end date.

(S-CDE) Is cardiovascular condition described above ongoing?

(C-CDE) Please describe constitutional symptoms indicated above. Include start/end date.

(S-CDE) Is constitutional symptoms condition described above ongoing?

(C-CDE) Please describe ears/nose/mouth/throat history indicated above. Include start/end date.

(S-CDE) Is ears/nose/mouth/throat condition described above ongoing?

(C-CDE) Please describe endocrine history indicated above. Include start/end date.

(S-CDE) Is endocrine condition described above ongoing?

(C-CDE) Please describe eye history indicated above. Include start/end date.

(S-CDE) Is eye condition described above ongoing?

(C-CDE) Please describe gastrointestinal history indicated above. Include start/end date.

(S-CDE) Is gastrointestinal condition described above ongoing?

(C-CDE) Please describe genitourinary history indicated above. Include start/end date.

(S-CDE) Is genitourinary condition described above ongoing?

(C-CDE) Please describe hematogenic/lymphatic history indicated above. Include start/end date.

(S-CDE) Is hematogenic/lymphatic condition described above ongoing?

(C-CDE) Please describe integumentary (skin and/or breast) history indicated above. Include start/end date.

(S-CDE) Is integumentary condition described above ongoing?

(C-CDE) Please describe musculoskeletal history indicated above. Include start/end date.

(S-CDE) Is musculoskeletal condition described above ongoing?

(C-CDE) Please describe neurological history indicated above. Include start/end date.

(S-CDE) Is neurological condition described above ongoing?

(C-CDE) Please describe psychiatric history indicated above. Include start/end date.

(S-CDE) Is psychiatric condition described above ongoing?

(C-CDE) Please describe respiratory history indicated above. Include start/end date.

(S-CDE) Is respiratory condition described above ongoing?

(C-CDE) Please describe "Other" history indicated above. Include start/end date.

(S-CDE) Is the "Other" condition described above ongoing?

(E-CDE) Types of cardiovascular conditions present before spinal cord lesion

(E-CDE) Cardiac pacemaker: date last inserted

(E-CDE) Please specify other cardiac disorders.

(E-CDE) Cardiac surgery: specify type of surgery or mechanical intervention the participant/patient underwent

(E-CDE) Cardiac surgery: date last performed

(E-CDE) Please specify Other selected above regarding cardiovascular history

(E-CDE) Pulmonary conditions present before the spinal cord lesion

(E-CDE) Please specify Other selected above regarding pulmonary history

(E-CDE) Endocrine & Metabolic conditions diagnosed before the spinal cord lesion

(E-CDE) Diabetes mellitus type

(E-CDE) Please specify lipid disorder

(E-CDE) Method used to diagnosis osteoporosis

(E-CDE) Please specify thyroid disease diagnosis

(E-CDE) Please specify Other selected above regarding endocrine and metabolic history

(E-CDE) Neuro-Musculoskeletal history before the spinal cord lesion

(E-CDE) Specifies name of pre-existing congenital deformity of the spine and spinal cord

(E-CDE) Anatomic site of pre-existing congenital deformity of spine and spinal cord

(E-CDE) Previous surgery due to congenital deformities of spine and spinal cord

(E-CDE) Date of surgery for congenital deformity
(E-CDE) Description of surgery caused by pre-existing congenital deformities of spine and spinal cord
(E-CDE) Specify name of pre-existing systemic neuro-degenerative disorder
(E-CDE) Specify location/anatomic site of pre-existing systemic neurodegenerative disorder
(E-CDE) Previous surgery due to neurodegenerative disorder
(E-CDE) Date of surgery caused by neurodegenerative disorder
(E-CDE) Description of surgery caused by neurodegenerative disorder
(E-CDE) Specify diagnosis of pre-existing degenerative spine disorder
(E-CDE) Specify location/anatomic site of pre-existing degenerative spine disorder
(E-CDE) Surgery due to degenerative spine disorder
(E-CDE) Date of surgery caused by degenerative spine disorder
(E-CDE) Description of surgery caused by degenerative spine disorder
(E-CDE) Urinary Tract Impairment before the spinal cord lesion
(E-CDE) Please specify
(E-CDE) Gastrointestinal or anal sphincter dysfunction before the spinal cord lesion
(E-CDE) Please specify

Prior and Concomitant Medications

(S-CDE) Did the patient take any medications prior to enrollment?
(S-CDE) Medication Name
(S-CDE) Reason For Administration of a Prior/Concomitant Agent or Measure
(S-CDE) Dose
(S-CDE) Frequency
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Route
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Start Date
(S-CDE) End Date
(S-CDE) Ongoing?
(S-CDE) Any Vasopressor Use
(S-CDE) Urinary Tract Drugs Within The Last Year
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Medication Affecting Bowel Function/Constipating Agents (Within the Last 4 Weeks):
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Medication Affecting Bowel Function- Oral Laxatives (Within the Last 4 Weeks):
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Medication Affecting Cardiovascular Function on the Day of Examination
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Treatment for Spasticity/Spasms Within the Last 4 Weeks
(S-CDE) Does the participant have any other serious co-morbid or concomitant medical condition that, in the opinion of the investigator, would compromise the safety of the patient/participant or compromise the participant's ability to participate in the study?

Alcohol and Tobacco Use

(S-CDE) How often do you have a drink containing alcohol?
(S-CDE) How often do you have five or more drinks on one occasion?
(S-CDE) Tobacco smoking history
(S-CDE) Which year did you quit smoking?
(S-CDE) For how many years did (have) you smoked
(S-CDE) On average, how many cigarettes do (did) you smoke on a daily basis?
(S-CDE) On average, how many cigars do (did) you smoke on a daily basis?

(S-CDE) On average, how many pipe bowls do (did) you smoke on a daily basis?

(S-CDE) Number of pack-years of smoking

Substance Use

(S-CDE) During the last 12 months (or during the time since your injury - if year 1 follow-up) did you use any illicit or non-prescription drugs?

(S-CDE) If Yes above, please indicate the drugs used

(S-CDE) List other drugs used

Family History

(E-CDE) Family History Medical Condition Types

(E-CDE) If indicated Other for previous question, please specify.

(E-CDE) Relationship of the Family Member or Ancestor with the Medical Condition or Health Related Event to the Participant

Trauma Characteristics

EMS History

(S-CDE) Date and Time first call received by EMS

(S-CDE) Date and Time of EMS dispatch

(S-CDE) EMS dispatch priority

(S-CDE) Type of EMS vehicle

(S-CDE) Date and Time of EMS arrival at scene

(S-CDE) Date and Time of EMS departure from scene

(S-CDE) Highest level of EMS service

Pre-Hospital Transport Time (Dispatch to Arrival)

(S-CDE) Date and time of EMS GCS

(S-CDE) GCS From EMS Report

(S-CDE) Best GCS Eye Response Score

(S-CDE) Best GCS Verbal Response Score

(S-CDE) Best GCS Motor Response Score

(S-CDE) AIS 6 Body Regions: Head & Neck

(S-CDE) AIS 6 Body Regions: Face

(S-CDE) AIS 6 Body Regions: Chest

(S-CDE) AIS 6 Body Regions: Abdomen

(S-CDE) AIS 6 Body Regions: Extremity

(S-CDE) AIS 6 Body Regions: External

(S-CDE) AIS 9 Body Regions: Head

(S-CDE) AIS 9 Body Regions: Neck

(S-CDE) AIS 9 Body Regions: Face

(S-CDE) AIS 9 Body Regions: Chest/Thorax

(S-CDE) AIS 9 Body Regions: Abdomen

(S-CDE) AIS 9 Body Regions: Spine

(S-CDE) AIS 9 Body Regions: Upper Extremity

(S-CDE) AIS 9 Body Regions: Lower Extremity

(S-CDE) AIS 9 Body Regions: External and Other

ED History

(S-CDE) ED Time of Arrival

(C-CDE) ED Date of Arrival

Transport Blood Pressure

Transport Heart Rate

(S-CDE) ISS Score on Arrival

(S-CDE) Intubated on Arrival

Total Time in ER

Time to OR

ED/EMS Description of Trauma

(C-CDE) ED ASIA Impairment Scale (AIS)

(C-CDE) ED Neurological Level of Injury
 ASIA Grade from PMR
 (C-CDE) Spinal Cord Injury Etiology
 Spinal Cord Injury Etiology Description
 (S-CDE) Iatrogenic Role in the Etiology
 (S-CDE) Timeframe of onset of NTSCI (non-traumatic spinal cord injury)
 (S-CDE) Classification of etiology of Non- Traumatic Spinal Cord Injury (NTSCI)- Axis 1- Level 1
 (S-CDE) Classification of etiology of Non- Traumatic Spinal Cord Injury (NTSCI)- Axis 1- Level 2
 (S-CDE) Classification of etiology of Non- Traumatic Spinal Cord Injury (NTSCI)- Axis 1- Level 3
 (S-CDE) Classification of etiology of Non- Traumatic Spinal Cord Injury (NTSCI)- Axis 1- Level 4
 (S-CDE) Classification of etiology of Non- Traumatic Spinal Cord Injury (NTSCI)- Axis 1- Level 5
 Working Diagnosis
 (S-CDE) Level of Care (provided to participant by health care facility)
 (S-CDE) ED GCS Score
 (C-CDE) Best GCS Eye Response Score
 (C-CDE) Best GCS Verbal Response Score
 (S-CDE) Best GCS Motor Response Score
 TBI Present?
 TBI Diagnosis
 Loss of Consciousness
 (S-CDE) Associated Injury (Includes moderate to severe traumatic brain injury[GCS< 12], non-vertebral fractures requiring surgery, severe facial injuries affecting sense organs, major chest injury requiring chest-tube or mechanical ventilation, traumatic amputations of an arm or leg (or injuries severe enough to require surgical amputation), severe hemorrhaging, or damage to any internal organ requiring surgery)
 Extremity Fractures
 (S-CDE) Penetrating/Blunt Injury
 Hemorrhagic Injury
 Central Cord Injury
 Cervical Injury
 Vertebral Fracture
 (S-CDE) Spinal Column Injury/ies (any disruption through the spinal column including the bony vertebral elements and their supporting ligaments, capsules, discs, and other supporting soft tissues)
 (S-CDE) Single or Multiple Spinal Column Level Injury/ies
 (S-CDE) Spinal Column Injury Level
 (S-CDE) Disc/Posterior Ligamentous Complex Injury
 (S-CDE) Traumatic Translation
 Peripheral Abrasions?
 Vertebral Artery Injury
 T2 Weighted Image
 History of Hypertension
 Patient History of Anti-coagulation Therapy
 Type of Anti-coagulation/Anti-Platelet Therapy
 Past History of TBI
 Past History of SCI
 (S-CDE) On Paralytics Pre-hospital Arrival
 (S-CDE) Sedated Pre-hospital Arrival
 (S-CDE) Hypotensive Episode Pre-hospital Arrival
 (S-CDE) Hypoxic Episode Pre-hospital Arrival

ED Rectal Tone

Neurological Exam

(CDE CORE) Date of Neurological Examination

(C-CDE) Sensory Level - Left

(C-CDE) Sensory Level - Right

(C-CDE) Motor Level - Left

(C-CDE) Motor Level – Right

ED Vitals

(S-CDE) Date Vitals Performed

(S-CDE) Time Examination Performed

(S-CDE) Height

(S-CDE) Weight

(S-CDE) Position During Blood Pressure Testing

(S-CDE) Compression Devices in Use During Testing

(S-CDE) Pulse

(S-CDE) Pulse Findings

(S-CDE) Blood Pressure - Systole

(S-CDE) Blood Pressure - Diastole

(S-CDE) Mean Arterial Pressure Measurement

(S-CDE) Temperature

(S-CDE) Method Temperature Measured

(S-CDE) Forced Vital Capacity (FVC)

(S-CDE) Forced Expiratory Volume in One Second (FEV1)

(S-CDE) Peak Expiratory Flow (PEF)

(S-CDE) Oxygen Saturation %

(S-CDE) Was a fasting lipid profile conducted while the patient was on anti-lipid therapy?

(E-CDE) Triglycerides (TG)

(E-CDE) LDL Cholesterol

(E-CDE) HDL Cholesterol

(E-CDE) Total Cholesterol (TC)

Blood Pressure Management

Hospital Blood Pressure Management

ICU MAP Goals

ICU Missed Map Goals

of PRBC Units Transfused

of Units of Blood Transfused

First Vasopressor Used

Max Dosage of Vasopressor 1

Was the Pressor Changed?

Second Vasopressor Used

Max Dosage of Vasopressor 2

2nd Vasopressor Added to the First?

Please Describe the Vasopressors Added Together

Two or More Vasopressors Used?

Dopamine Complications

Neo Complications

(S-CDE) ED Hypotension (Systolic < 100)

(S-CDE) ED Hypotension (Systolic < 90)

(S-CDE) ED Hypotension (Systolic < 80)

(S-CDE) ED Hypotension (Systolic < 70)

ED Bradycardia

ED Fluid Bolus
ED Vasopressor Given
(S-CDE) OR Hypotension (Systolic < 100)
(S-CDE) OR Hypotension (Systolic < 90)
Upload ICU MAP

Operating Room

SCI OR Procedures

Date of Last Surgical Intervention
SCI Surgical Procedure 1 Name
SCI Surgical Procedure 1 CPT
SCI Surgical Procedure 2 Name
SCI Surgical Procedure 2 CPT
SCI Surgical Procedure 3 Name
SCI Surgical Procedure 3 CPT
Age At Time of Surgery
Surgery Date
Patient Weight
Format of the operation room in the Anesthesia Report for the subject's operation
Format A: Time in which anesthesia care is started
Format A: Time in which anesthesia care ends
Format A: Time induction is started on the patient
Format A: Time in which induction ends
Format A: Procedure start time on patient
Format A: Procedure end time on patient
Format A: Time that all OR tasks end
Format B: Anesthesia care start time
Format B: Anesthesia end time
Format B: Time in which anesthesia starts in the OR
Format B: Time in which anesthesia leaves the OR
Format B: Time in which anesthesia ends in the OR
Format A & B: Time in which first incision was made
Closure Time
Total time from procedure start to procedure end (minutes)
Type of surgery patient underwent. Types include Spinal Cord Injury [SCI]: Laminectomy and Non-SCI.
Polytrauma noted in OR report
Method used for intubation
ABG lab value for partial pressure of oxygen - Reading 1
ABG lab value for partial pressure of oxygen - Reading 2
ABG lab value for partial pressure of oxygen - Reading 3
ABG lab value for partial pressure of oxygen - Reading 4
ABG lab value for partial pressure of oxygen - Reading 5
ABG lab value for partial pressure of oxygen - Reading 6
ABG lab value for partial pressure of oxygen - Reading 7
ABG lab value for partial pressure of oxygen - Reading 8
ABG lab value for partial pressure of oxygen - Reading 9
ABG lab value for partial pressure of oxygen - Reading 10

Anesthesia

Whether a steroid was used in the operation

Steroid Type

Pre-operative Hematocrit

Type of vasopressor used during the surgery

Patient received Phenylephrine as a vasopressor during the operation (Includes Neosynephrine)

Patient received Dopamine as a vasopressor during the operation

Patient received Norepinephrine as a vasopressor during the operation (Includes Levophed)

Type of anesthesia used during surgery

Packed red blood cell's [PRBC] given to patient during surgery

Crystalloids given to patient during surgery

Lab value of hematocrit obtained at some point during surgery

Upload OR Time Specific Data

Additional OR information regarding the patient

Interventions

Hospital Interventions

(S-CDE) Admitted to Special Care Unit at Any Time During Their Stay (Includes ICU and Step-Down Units)

(S-CDE) Type of Special Care Unit

(S-CDE) Special Care Unit Admission Date

Special Care Unit Admission Time

History of Present Illness

Bolt (ICP) Placement

EVD Placement

Lumbar Drain Placement

Spinal Surgery

Other Surgical Interventions

Methylprednisolone/Steroid Treatment?

Please specify Other indicated above

(S-CDE) Date(s) Steroid Administered

Neuro-Monitoring?

Neuro-Monitoring Alarm During Procedure?

Neuro-Monitoring Notes

Anesthesia

OR MAP

Current levels wrist

Current level ankle

Baseline LN20

Baseline RN20

Baseline LP45

Baseline RP45

Baseline Volts Lupper

Baseline Volts Rupper

Baseline Volts Llower

Baseline Volts Rlower

End SSEP LN20

End SSEP RN20

End SSEP Lp45

End SSEP Rp45

End Volts Lupper

End Volts Rupper

End Volts Llower

End Volts Rlower

Signal Quality

SSEP compared to exam
MEP compared to exam
Restraints Utilized/Required
Intubation
Reintubation
Ventilatory Assistance Utilized
Please specify Other indicated above
Number of Days on Ventilator
Tracheostomy
Gastrostomy/PEG
Central Venous Cath
Peripheral Inserted Central Cath (PICC)
Arterial Line
Renal Replacement Therapy
Reversal of Coagulopathy on Admission?
ECG Notes

Muscle and Sensory Exams

Neurosurgery Service Consult

Neurosurgery Service Consult
Neurosurgery Consult Date
Neurosurgery Consult Time
Left Bicep Strength
Left Deltoid Strength
Left EHL Strength
Left Gastro Strength
Left Grip Strength
Left Hamstring Strength
Left Interos Strength
Left IP Strength
Left Quad Strength
Left TA Strength
Left Tricep Strength
Left WE Strength
Left WF Strength
Right Bicep Strength
Right Deltoid Strength
Right EHL Strength
Right Gastro Strength
Right Grip Strength
Right Hamstring Strength
Right Interos Strength
Right IP Strength
Right Quad Strength
Right TA Strength
Right Tricep Strength
Right WE Strength
Right WF Strength

ISNCSCI Exam

Was ISNCSCI Completed?
(C-CDE) Date of Exam
(C-CDE) Time of Exam
(C-CDE) Neurological Level of Injury
(C-CDE) Complete or Incomplete?
(C-CDE) ASIA Impairment Scale
(C-CDE) Sensory Neurological Level - Right
(C-CDE) Sensory Neurological Level - Left

(C-CDE) Motor Neurological Level - Right
(C-CDE) Motor Neurological Level - Left
(C-CDE) Motor Upper Limb Subtotal - Right
(C-CDE) Motor Upper Limb Subtotal - Left
(C-CDE) Motor Upper Limb Total - Right + Left
(C-CDE) Motor Lower Limb Subtotal - Right
(C-CDE) Motor Lower Limb Subtotal - Left
(C-CDE) Motor Lower Limb Total - Right + Left
(C-CDE) Sensory Light Touch Subtotal - Right
(C-CDE) Sensory Light Touch Subtotal - Left
(C-CDE) Sensory Light Touch Total - Right + Left
(C-CDE) Sensory Pin Prick Subtotal - Right
(C-CDE) Sensory Pin Prick Subtotal - Left
(C-CDE) Sensory Pin Prick Total - Right + Left
(C-CDE) Voluntary Anal Contraction (VAC)
(C-CDE) Any Anal Sensation
(C-CDE) Zone of Partial Preservation: Motor Right
(C-CDE) Zone of Partial Preservation: Motor Left
(C-CDE) Zone of Partial Preservation: Sensory Right
(C-CDE) Zone of Partial Preservation: Sensory Left
(C-CDE) Motor Elbow Flexors - Right
(C-CDE) Motor Wrist Extensors - Right
(C-CDE) Motor Elbow Extensors - Right
(C-CDE) Motor Finger Flexors - Right
(C-CDE) Motor Finger Abductors - Right
(C-CDE) Motor Hip Flexors - Right
(C-CDE) Motor Knee Extensors - Right
(C-CDE) Motor Ankle Dorsiflexors - Right
(C-CDE) Motor Long Toe Extensors - Right
(C-CDE) Motor Ankle Plantar Flexors - Right
(C-CDE) Motor Elbow Flexors - Left
(C-CDE) Motor Wrist Extensors - Left
(C-CDE) Motor Elbow Extensors - Left
(C-CDE) Motor Finger Flexors - Left
(C-CDE) Motor Finger Abductors - Left
(C-CDE) Motor Hip Flexors - Left
(C-CDE) Motor Knee Extensors - Left
(C-CDE) Motor Ankle Dorsiflexors - Left
(C-CDE) Motor Long Toe Extensors - Left
(C-CDE) Motor Ankle Plantar Flexors - Right
(C-CDE) Sensory Light Touch C2 - Right
(C-CDE) Sensory Light Touch C3 - Right
(C-CDE) Sensory Light Touch C4 - Right
(C-CDE) Sensory Light Touch C5 - Right
(C-CDE) Sensory Light Touch C6 - Right
(C-CDE) Sensory Light Touch C7 - Right
(C-CDE) Sensory Light Touch C8 - Right
(C-CDE) Sensory Light Touch T1 - Right
(C-CDE) Sensory Light Touch T2 - Right
(C-CDE) Sensory Light Touch T3 - Right
(C-CDE) Sensory Light Touch T4 - Right
(C-CDE) Sensory Light Touch T5 - Right
(C-CDE) Sensory Light Touch T6 - Right
(C-CDE) Sensory Light Touch T7 - Right
(C-CDE) Sensory Light Touch T8 - Right
(C-CDE) Sensory Light Touch T9 - Right
(C-CDE) Sensory Light Touch T10 - Right

(C-CDE) Sensory Light Touch T11 - Right
(C-CDE) Sensory Light Touch T12 - Right
(C-CDE) Sensory Light Touch L1 - Right
(C-CDE) Sensory Light Touch L2 - Right
(C-CDE) Sensory Light Touch L3 - Right
(C-CDE) Sensory Light Touch L4 - Right
(C-CDE) Sensory Light Touch L5 - Right
(C-CDE) Sensory Light Touch S1 - Right
(C-CDE) Sensory Light Touch S2 - Right
(C-CDE) Sensory Light Touch S3 - Right
(C-CDE) Sensory Light Touch S4-5 - Right
(C-CDE) Sensory Pin Prick C2 - Right
(C-CDE) Sensory Pin Prick C3 - Right
(C-CDE) Sensory Pin Prick C4 - Right
(C-CDE) Sensory Pin Prick C5 - Right
(C-CDE) Sensory Pin Prick C6 - Right
(C-CDE) Sensory Pin Prick C7 - Right
(C-CDE) Sensory Pin Prick C8 - Right
(C-CDE) Sensory Pin Prick T1 - Right
(C-CDE) Sensory Pin Prick T2 - Right
(C-CDE) Sensory Pin Prick T3 - Right
(C-CDE) Sensory Pin Prick T4 - Right
(C-CDE) Sensory Pin Prick T5 - Right
(C-CDE) Sensory Pin Prick T6 - Right
(C-CDE) Sensory Pin Prick T7 - Right
(C-CDE) Sensory Pin Prick T8 - Right
(C-CDE) Sensory Pin Prick T9 - Right
(C-CDE) Sensory Pin Prick T10 - Right
(C-CDE) Sensory Pin Prick T11 - Right
(C-CDE) Sensory Pin Prick T12 - Right
(C-CDE) Sensory Pin Prick L1 - Right
(C-CDE) Sensory Pin Prick L2 - Right
(C-CDE) Sensory Pin Prick L3 - Right
(C-CDE) Sensory Pin Prick L4 - Right
(C-CDE) Sensory Pin Prick L5 - Right
(C-CDE) Sensory Pin Prick S1 - Right
(C-CDE) Sensory Pin Prick S2 - Right
(C-CDE) Sensory Pin Prick S3 - Right
(C-CDE) Sensory Pin Prick S4-5 - Right
(C-CDE) Sensory Light Touch C2 - Left
(C-CDE) Sensory Light Touch C3 - Left
(C-CDE) Sensory Light Touch C4 - Left
(C-CDE) Sensory Light Touch C5 - Left
(C-CDE) Sensory Light Touch C6 - Left
(C-CDE) Sensory Light Touch C7 - Left
(C-CDE) Sensory Light Touch C8 - Left
(C-CDE) Sensory Light Touch T1 - Left
(C-CDE) Sensory Light Touch T2 - Left
(C-CDE) Sensory Light Touch T3 - Left
(C-CDE) Sensory Light Touch T4 - Left
(C-CDE) Sensory Light Touch T5 - Left
(C-CDE) Sensory Light Touch T6 - Left
(C-CDE) Sensory Light Touch T7 - Left
(C-CDE) Sensory Light Touch T8 - Left
(C-CDE) Sensory Light Touch T9 - Left
(C-CDE) Sensory Light Touch T10 - Left
(C-CDE) Sensory Light Touch T11 - Left

(C-CDE) Sensory Light Touch T12 - Left
(C-CDE) Sensory Light Touch L1 - Left
(C-CDE) Sensory Light Touch L2 - Left
(C-CDE) Sensory Light Touch L3 - Left
(C-CDE) Sensory Light Touch L4 - Left
(C-CDE) Sensory Light Touch L5 - Left
(C-CDE) Sensory Light Touch S1 - Left
(C-CDE) Sensory Light Touch S2 - Left
(C-CDE) Sensory Light Touch S3 - Left
(C-CDE) Sensory Light Touch S4-5 - Left
(C-CDE) Sensory Pin Prick C2 - Left
(C-CDE) Sensory Pin Prick C3 - Left
(C-CDE) Sensory Pin Prick C4 - Left
(C-CDE) Sensory Pin Prick C5 - Left
(C-CDE) Sensory Pin Prick C6 - Left
(C-CDE) Sensory Pin Prick C7 - Left
(C-CDE) Sensory Pin Prick C8 - Left
(C-CDE) Sensory Pin Prick T1 - Left
(C-CDE) Sensory Pin Prick T2 - Left
(C-CDE) Sensory Pin Prick T3 - Left
(C-CDE) Sensory Pin Prick T4 - Left
(C-CDE) Sensory Pin Prick T5 - Left
(C-CDE) Sensory Pin Prick T6 - Left
(C-CDE) Sensory Pin Prick T7 - Left
(C-CDE) Sensory Pin Prick T8 - Left
(C-CDE) Sensory Pin Prick T9 - Left
(C-CDE) Sensory Pin Prick T10 - Left
(C-CDE) Sensory Pin Prick T11 - Left
(C-CDE) Sensory Pin Prick T12 - Left
(C-CDE) Sensory Pin Prick L1 - Left
(C-CDE) Sensory Pin Prick L2 - Left
(C-CDE) Sensory Pin Prick L3 - Left
(C-CDE) Sensory Pin Prick L4 - Left
(C-CDE) Sensory Pin Prick L5 - Left
(C-CDE) Sensory Pin Prick S1 - Left
(C-CDE) Sensory Pin Prick S2 - Left
(C-CDE) Sensory Pin Prick S3 - Left
(C-CDE) Sensory Pin Prick S4-5 – Left

Hospital Outcomes

Patient Hospital Outcomes

(S-CDE) Discharge Location Type
Discharge Location
(C-CDE) Facility Discharge Date
(S-CDE) Facility Discharge Time
ICU Care
ICU Length of Stay
(C-CDE) Hospital Length of Stay
(S-CDE) Vital Status on Discharge
(C-CDE) ASIA Grade on Discharge
Degree Of ASIA Improvement
(S-CDE) Utilization of Ventilator Assistance on Discharge
Stroke
Alcohol Withdrawal
Pneumonia
Respiratory Failure
UTI

Acute Renal Insufficiency
Central Venous Catheter Infection
Surgical Site Infection
DVT
Pulmonary Embolism
GCS On Discharge
Best GCS Eye Response Score
Best GCS Verbal Response Score
Best GCS Motor Response Score
(C-CDE) Date of Final Inpatient Neurological Exam
(C-CDE) Sensory Level - Left
(C-CDE) Sensory Level - Right
(C-CDE) Motor Level - Left
(C-CDE) Motor Level - Right
Wound Complications
Additional Notes

Imaging

MRI

MRI Imaging?
(S-CDE) MRI Study Date and Time
Hours to MRI
(S-CDE) MR Anatomic Area
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Imaging Scanner Manufacturer Name
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Imaging Scanner Model Name
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Imaging Scanner Strength
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) Imaging Scanner Software Version Number
(S-CDE) Image Quality
MRI T2 Axial Available?
Upload T2 Axial File
MRI T2 Sagittal Available?
Upload T2 Sagittal
MRI T2 MERGE Available?
Upload T2 MERGE
MRI T2 Diffusion Available?
Upload T2 Diffusion
MRI Additional Imaging Modality?
MRI MSCC
MRI MCC
Long Extent of T2 Signal
Sag Grade
MRI BASIC Score
Macroscopic Hemorrhage Present?
Epicenter Cord Surface Area (CSA)
Percentage White Matter T2 Hyperintensity
Percentage Grey Matter
(S-CDE) Pre-Existing Hardware/Surgery?
(S-CDE) Type of Pre-Existing Hardware/Surgery
(S-CDE) If indicated Other for previous question, please specify.
(S-CDE) If yes, provide an upper limit of instrumentation
(S-CDE) Lower limit
(S-CDE) Exam pulse sequence inventory
(S-CDE) Exam pulse sequence inventory

(S-CDE) Injury type
 (S-CDE) Subluxation/translation level
 (S-CDE) Measure of subluxation from posterior aspect of vertebral body relative to nearest adjacent body
 (S-CDE) Angulation level
 (S-CDE) Extra-axial fluid upper limit
 (S-CDE) Extra-axial fluid lower limit
 (S-CDE) Extra-axial fluid point of maximum compression
 (S-CDE) Vertebral fracture upper level
 (S-CDE) Vertebral fracture lower level
 (S-CDE) Traumatic herniated nucleus pulposus (HNP) level
 (S-CDE) Traumatic herniated nucleus pulposus (HNP) type
 (S-CDE) Ligamentous injury/rupture
 (S-CDE) Ligamentous injury/rupture
 (S-CDE) Ligamentous injury/rupture level
 (S-CDE) Degenerative features
 (S-CDE) Degenerative features indicator
 (S-CDE) Provide the upper limit of abnormality
 (S-CDE) Lower limit
 (S-CDE) Canal/cord measurements type
 (S-CDE) Sagittal canal diameter rostral injury
 (S-CDE) Sagittal canal diameter injury
 (S-CDE) Sagittal canal diameter caudal to injury
 (S-CDE) Cord diameter rostral to injury sagittal
 (S-CDE) Spinal cord diameter rostral to injury transverse
 (S-CDE) Cord diameter injury sagittal
 (S-CDE) Cord diameter injury transverse
 (S-CDE) Cord diameter caudal sagittal
 (S-CDE) Cord diameter caudal transverse
 (S-CDE) Level
 (S-CDE) Acute ACI features
 (S-CDE) Level [Range4 FM-L3.3]
 (S-CDE) Integer range [1-50]
 (S-CDE) Cord transection
 (S-CDE) Chronic SCI features
 (S-CDE) Chronic SCI feature indicator
 (S-CDE) Upper level [Range4 FM-L3]
 (S-CDE) Lower level [Range4 FM-L3]
 (S-CDE) Caliber [Integer range 1-10]
 (S-CDE) Length [Integer range 1-60]
 Dates of Additional MRIs

CT

CT Available?
 (S-CDE) CT Study Date and Time
 Number of CT Scans
 Dates of CT Scans
 CTA Available
 Number of CTA Scans
 Dates of CTA Scans
 DTI Available?

DTI

(S-CDE) DTI Study Date and Time
 (S-CDE) Name of Scanner Manufacturer
 (S-CDE) If indicated Other for previous question, please specify.
 (S-CDE) Name of scanner software that runs the imaging camera
 (S-CDE) Version number of the imaging scanner software
 (S-CDE) Magnetic Field Strength of Scanner Used
 (S-CDE) If indicated Other for previous question, please specify.

(S-CDE) Imaging Pulse Sequence Used
(S-CDE) Slide Orientation
(S-CDE) Frame of Reference
(S-CDE) Repetition Time (TR)
(S-CDE) Echo time (TE)
(S-CDE) FA
(S-CDE) Freq FOV mm
(S-CDE) Matrix Size (Axis 1)
(S-CDE) Matrix Size (Axis 2)
(S-CDE) Number of Slices
(S-CDE) Slice Thickness
(S-CDE) Slice Gap
(S-CDE) Voxel Size (Axis 1)
(S-CDE) Voxel Size (Axis 2)
(S-CDE) Voxel Size (Axis 3)
(S-CDE) NEX
(S-CDE) Phase-encode direction
(S-CDE) Was fat signal suppressed in imaging acquisition?
(S-CDE) Band Width
(S-CDE) 2DRF Tilt Angle
(S-CDE) Was flow compensation used in imaging acquisition?
(S-CDE) Echo Train Length
(S-CDE) b-value (first)
(S-CDE) b-value (second)
(S-CDE) b-value (third)
(S-CDE) b-value (fourth)

Other

Imaging Notes

Follow Up Measures

Urodynamics Data Set

Urodynamic Questionnaire Completed?
(S-CDE) Date and Time of Data Collection
(S-CDE) Bladder Sensation During Filling Cystometry
(S-CDE) Detrusor Function
(S-CDE) Bladder Compliance During Filling Cystometry
(S-CDE) Urethral Function During Voiding
(S-CDE) Detrusor Leak Point Pressure During Filling Cystometry
(S-CDE) Maximum Detrusor Pressure Filing Cystometry
(S-CDE) Cystometric Bladder Capacity During Filling Cystometry
(S-CDE) Post Void Residual Volume

Lower Urinary Tract Function Data Set

Lower Urinary Tract Function Questionnaire Completed?
Date and Time of Data Collection
(S-CDE) Urinary tract impairment unrelated to spinal cord lesion
(S-CDE) If indicated Yes above, please specify.
(S-CDE) Awareness of the need to empty the bladder
(S-CDE) If indicated Yes for previous question, please specify
(S-CDE) Main bladder emptying
(S-CDE) Supplementary bladder emptying
(S-CDE) Average number of voluntary bladder emptyings per day during the last week
(S-CDE) Any involuntary urine leakage (incontinence) within the last three months
(S-CDE) Collecting appliances for urinary incontinence
(S-CDE) If indicated Other for previous question, please specify
(S-CDE) Any drugs for the urinary tract within the last year
(S-CDE) If indicated Other for previous question, please specify
(S-CDE) Surgical procedures on the urinary tract?

(S-CDE) If Yes for previous question, what surgical procedures on the urinary tract have been done?

(S-CDE) If indicated Other for previous question, please specify

(S-CDE) Date(s) performed

(S-CDE) Any change in urinary symptoms within the last year

Urinary Tract Infection

Urinary Tract Infection Questionnaire Completed?

(S-CDE) Date and Time of Data Collection

(S-CDE) Length of Time of Sign(s)/Symptoms(s)

(S-CDE) Sign(s)/symptom(s)

(S-CDE) If indicated Other for previous question, please specify

(S-CDE) Urine dipstick test for nitrite

(S-CDE) Urine dipstick test for leukocyte esterase

(S-CDE) Urinary culture

(S-CDE) Urine culture sequence number

(S-CDE) Species

(S-CDE) Colony Forming Units (CFU) per mL

(S-CDE) The resistance pattern

Bowel Function Data Set

Bowel Function Questionnaire Completed?

(S-CDE) Date and Time of Data Collection

(S-CDE) Administration Method

(S-CDE) Duration of constipation

(S-CDE) Unsuccessful attempts at defecation within the last three months

(S-CDE) Incomplete rectal emptying after defecation within the last three months

(S-CDE) Abdominal bloating within the last three months

(S-CDE) Abdominal pain/discomfort within the last three months

(S-CDE) Any respiratory discomfort shortness of breath difficulty in taking a deep breath considered to be entirely or partly due to a distended abdomen within the last three months

(S-CDE) Perianal pain during defecation within the last three months

(S-CDE) Frequency of flatus incontinence within the last three months

(S-CDE) Frequency of incontinence to liquid stools within the last three months

(S-CDE) Frequency of incontinence to solid stools within the last three months

(S-CDE) Ability to defer defecation for fifteen minutes or more within the last three months

(S-CDE) Position for bowel care within the last three months

(S-CDE) If indicated Other for previous question, please specify.

(S-CDE) Degree of independency during bowel management within the last three months

(S-CDE) Bowel care facilitators within the last three months

(S-CDE) If indicated Other for previous question, please specify.

(S-CDE) Events and intervals of defecation (1): Average time from initiation of bowel care to stool comes out within the last three months

(S-CDE) Events and intervals of defecation (2): Average time during bowel movement that stool intermittently or continuously comes out with or without assistance within the last three months

(S-CDE) Events and intervals of defecation (3): Average time spent waiting after last stool passes before ending bowel care within the last three months

(S-CDE) Lifestyle alteration due to anal incontinence within the last three months

(S-CDE) Lifestyle alteration due to constipation within the last three months

(S-CDE) Self reported impact on quality of life due to bowel dysfunction

(S-CDE) Anal tone

(S-CDE) Voluntary contraction of the anal canal

Spinal Intervention and Spinal Procedures Data Set

Spinal Intervention and Spinal Procedures Questionnaire Completed?

(S-CDE) Intervention/procedure date and start time:

(S-CDE) Non-surgical bed rest and external immobilization:

(S-CDE) Spinal intervention - closed manipulation and/or reduction of spinal elements:

(S-CDE) Spinal procedure - approach:

(S-CDE) Date and Time of the Intervention Completion or Surgical Closure:

(S-CDE) Surgical procedure - open reduction:

(S-CDE) Surgical procedure - direct decompression of neural elements:

(S-CDE) Surgical procedure - stabilization and fusion: (one to be filled in for each level of injury, starting with the most cephalic injury)

Stabilization and Fusion - Segment Number

(S-CDE) Surgical procedure – stabilization and fusion: (one to be filled in for each level of injury, starting with the most cephalic injury):

Stabilization and Fusion – Segment Level

Upper Extremity Data Set

SCI Upper Extremity Questionnaire Completed?

(S-CDE) Date and Time of Data Collection

(S-CDE) Laterality

Basic Right Hand - Ability to reach and grasp

Basic Right Hand - Shoulder function classification

Basic Left Hand - Ability to reach and grasp

Basic Left Hand - Shoulder function classification

(S-CDE) Use of assistive devices used to enhance upper extremity function

(S-CDE) Complications to upper extremity function like pain, spasms, contractures, edema, etc

(S-CDE) Upper Extremity/Hand Reconstructive Surgery

(S-CDE) Type of surgery

(S-CDE)Specify "Soft tissue reconstruction: Other" indicated above

(S-CDE)Specify "Other" indicated above

(S-CDE) Specify "Implantable FES" indicated above

(S-CDE) Date of surgery(s)

Cardiovascular Function Data Set

Cardiovascular Function Questionnaire Completed?

Date and Time of Data Collection

(S-CDE) Cardiovascular history before spinal cord lesion

(S-CDE) If indicated Other for previous question, please specify

(S-CDE) Events related to cardiovascular function after spinal cord lesion

(S-CDE) If indicated Other for previous question, please specify

(S-CDE) Cardiovascular function after spinal cord lesion within the last three months

If indicated Cardiac Conditions for previous question, please specify

(S-CDE) If indicated Other for previous question, please specify

(S-CDE) Any medication affecting cardiovascular function on the day of examination

(S-CDE) If indicated Other for previous question, please specify

(S-CDE) Time performed

(S-CDE) Position during testing

(S-CDE) Devices in use during testing

(S-CDE) Pulse

(S-CDE) Pulse Regularity

(S-CDE) Systolic Blood Pressure

(S-CDE) Diastolic Blood Pressure

Sexual Function Data Set

Sexual Function Questionnaire Completed?

(S-CDE) Date and Time of Data Collection

(S-CDE) Interest in discussing sexual issues

(S-CDE) Sexual problems unrelated to spinal cord lesion

(S-CDE) If answered yes above, please specify:

(S-CDE) Sexual dysfunction related to the spinal cord lesion:

(S-CDE) [FEMALE-ONLY] Psychogenic genital arousal

(S-CDE) [FEMALE-ONLY] Reflex genital arousal

(S-CDE) [FEMALE-ONLY] Menstruation

(S-CDE) [MALE-ONLY] Psychogenic Erection

(S-CDE) [MALE-ONLY] Reflex Erection

(S-CDE) [MALE-ONLY] Ejaculation

(S-CDE) [BOTH] Orgasmic function

Quality of Life Data Set

Quality of Life Questionnaire Completed

(S-CDE) Date and Time of Data Collection

(S-CDE) Thinking about your own life and personal circumstances, how satisfied are you with your life as a whole in the past four weeks? Please use a scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied). You can use 0 or 10 or any number in between.

(S-CDE) How satisfied are you with your physical health in the past four weeks? Please use a scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied). You can use 0 or 10 or any number in between.

(S-CDE) How satisfied are you with your psychological health, emotions and mood in the past four weeks? Please use a scale ranging from 0 (completely dissatisfied) to 10 (completely satisfied). You can use 0 or 10 or any number in between.

(S-CDE) I can keep up with my family responsibilities...

(S-CDE) I am able to do all of my regular family activities...

(S-CDE) I am able to socialize with my friends...

(S-CDE) I am able to do all of my regular activities with friends...

(S-CDE) I can keep up with my social commitments...

(S-CDE) I am able to participate in leisure activities...

(S-CDE) I am able to perform my daily routines...

(S-CDE) I can keep up with my work responsibilities (include work at home)...

(S-CDE) I am able to do all of the family activities that people expect me to do...

(S-CDE) I am able to do all of the family activities that I want to do...

(S-CDE) I am able to maintain my friendships as much as I would like...

(S-CDE) I can do everything for my friends that I want to do...

(S-CDE) I am able to do all of the activities with friends that people expect me to do...

(S-CDE) I am able to do all of the activities with friends that I want to do...

(S-CDE) I am able to do all of my regular leisure activities...

(S-CDE) I am able to do my hobbies or leisure activities...

(S-CDE) I am able to do all of the community activities that I want to do...

(S-CDE) I am able to do all of the leisure activities that people expect me to do...

(S-CDE) I can do all the leisure activities that I want to do...

(S-CDE) I am able to do all of the community activities that people expect me to do...

(S-CDE) I am able to go out for entertainment as much as I want...

(S-CDE) I am able to run errands without difficulty...

(S-CDE) I am able to do all of my usual work (include work at home)...

(S-CDE) I am accomplishing as much as usual at work for me (include work at home)...

(S-CDE) My ability to do my work is as good as it can be (include work at home)...

(S-CDE) I can do everything for work that I want to do (include work at home)...

(S-CDE) I am able to do all of the work that people expect me to do (include work at home)

(S-CDE) I am able to do all of my usual work...

(S-CDE) I am able to do all of the work that people expect me to do...

(S-CDE) I have to do my work for shorter periods of time than usual for me...

(S-CDE) I have trouble meeting the needs of my family...

(S-CDE) I have to limit my regular family activities...

(S-CDE) I feel limited in my ability to visit friends...

(S-CDE) I feel limited in the amount of time I have to visit friends...

(S-CDE) I have to limit the things I do for fun at home (like reading, listening to music, etc.)...

(S-CDE) I have to limit my hobbies or leisure activities...

(S-CDE) I have to do my hobbies or leisure activities for shorter periods of time than usual for me...

(S-CDE) I have to limit social activities outside my home...

(S-CDE) I have trouble keeping in touch with others...

(S-CDE) I have to limit the things I do for fun outside my home...

(S-CDE) I am doing fewer social activities with groups of people than usual for me...

(S-CDE) I have trouble doing my regular chores or tasks...

(S-CDE) I am limited in doing my work (include work at home)...

(S-CDE) I have to do my work for shorter periods of time than usual for me (include work at home)...

(S-CDE) I am limited in doing my work...

(S-CDE) I felt uneasy...

(S-CDE) I felt nervous...

(S-CDE) Many situations made me worry...

(S-CDE) My worries overwhelmed me...

(S-CDE) I felt tense...

(S-CDE) I had difficulty calming down...

(S-CDE) I had sudden feelings of panic...

(S-CDE) I felt nervous when my normal routine was disturbed...

(S-CDE) I felt fearful about my future...

(S-CDE) I felt anxious...

(S-CDE) I worried about my physical health...

(S-CDE) I felt like I needed help for my anxiety...

(S-CDE) I was easily startled...

(S-CDE) I felt fidgety...

(S-CDE) I felt something awful would happen...

(S-CDE) I felt worried...

(S-CDE) I suddenly felt scared for no reason...

(S-CDE) I worried about dying...

(S-CDE) I felt shy...

(S-CDE) I had difficulty sleeping...

(S-CDE) I had trouble relaxing...

(S-CDE) I felt depressed...

(S-CDE) I felt hopeless...

(S-CDE) I felt that nothing could cheer me up...

(S-CDE) I felt that my life was empty...

(S-CDE) I felt worthless...

(S-CDE) I felt unhappy...

(S-CDE) I felt I had no reason for living...

(S-CDE) I felt that nothing was interesting...

(S-CDE) I felt helpless...

(S-CDE) I felt that I wanted to give up on everything...

(S-CDE) I felt that I had nothing to look forward to...

(S-CDE) I withdrew from other people...

(S-CDE) I felt that everything I did was an effort...

(S-CDE) I was critical of myself for my mistakes...

(S-CDE) I felt sad...

(S-CDE) I felt lonely...

(S-CDE) I felt discouraged about the future...

(S-CDE) I found that things in my life were overwhelming...

(S-CDE) I felt unloved...

(S-CDE) I felt pessimistic...

(S-CDE) I had trouble keeping my mind on what I was doing...

(S-CDE) I felt emotionally exhausted...

(S-CDE) I felt like I needed help for my depression...

(S-CDE) I had trouble enjoying things that I used to enjoy...

(S-CDE) I had trouble controlling my temper...

(S-CDE) It was hard to control my behavior...

(S-CDE) I said or did things without thinking...

(S-CDE) I got impatient with other people...

(S-CDE) I was irritable around other people...

(S-CDE) I was bothered by little things...

(S-CDE) I became easily upset...

(S-CDE) I was in conflict with others...

(S-CDE) I felt impulsive...

(S-CDE) People told me that I talked in a loud or excessive manner...

(S-CDE) I said or did things that other people probably thought were inappropriate...

(S-CDE) I felt angry...

(S-CDE) I suddenly became emotional for no reason...

(S-CDE) I felt restless...

(S-CDE) It was hard to adjust to unexpected changes...
 (S-CDE) I had a hard time accepting criticism from other people...
 (S-CDE) I was stubborn with others...
 (S-CDE) I threatened violence toward people or property...
 (S-CDE) I felt exhausted...
 (S-CDE) I felt that I had no energy...
 (S-CDE) I felt fatigued...
 (S-CDE) I was too tired to do my household chores...
 (S-CDE) I was too tired to leave the house...
 (S-CDE) I was frustrated by being too tired to do the things I wanted to do...
 (S-CDE) I felt tired...
 (S-CDE) I had to limit my social activity because I was tired...
 (S-CDE) I needed help doing my usual activities because of my fatigue...
 (S-CDE) I needed to sleep during the day...
 (S-CDE) I had trouble starting things because I was too tired...
 (S-CDE) I had trouble finishing things because I was too tired...
 (S-CDE) I was too tired to take a short walk...
 (S-CDE) I was too tired to eat...
 (S-CDE) I was so tired that I needed to rest during the day...
 (S-CDE) I felt weak all over...
 (S-CDE) I needed help doing my usual activities because of weakness...
 (S-CDE) I had to limit my social activity because I was physically weak...
 (S-CDE) I had to force myself to get up and do things because I was physically too weak..
 (S-CDE) Are you able to get on and off the toilet?
 (S-CDE) Are you able to step up and down curbs?
 (S-CDE) Are you able to get in and out of a car?
 (S-CDE) Are you able to get out of bed into a chair?
 (S-CDE) Are you able to push open a heavy door?
 (S-CDE) Are you able to run errands and shop?
 (S-CDE) Are you able to get up off the floor from lying on your back without help?
 (S-CDE) Are you able to go for a walk of at least 15 minutes?
 (S-CDE) How much DIFFICULTY do you currently have standing up from an armless straight chair (e.g., dining room chair)?
 (S-CDE) How much DIFFICULTY do you currently have sitting down on and standing up from a chair with arms?
 (S-CDE) How much DIFFICULTY do you currently have moving from sitting at the side of the bed to lying down on your back?
 (S-CDE) How much DIFFICULTY do you currently have standing up from a low, soft couch?
 (S-CDE) How much DIFFICULTY do you currently have going up and down a flight of stairs inside, using a handrail?
 (S-CDE) How much DIFFICULTY do you currently have walking on uneven surfaces (e.g., grass, dirt road or sidewalk)?
 (S-CDE) How much DIFFICULTY do you currently have walking around one floor of your home?
 (S-CDE) How much DIFFICULTY do you currently have taking a 20-minute brisk walk, without stopping to rest?
 (S-CDE) How much DIFFICULTY do you currently have walking on a slippery surface, outdoors?
 (S-CDE) How much DIFFICULTY do you currently have climbing stairs step over step without a handrail? (alternating feet)?
 (S-CDE) How much DIFFICULTY do you currently have walking in a dark room without falling?
 (S-CDE) I had a sense of well-being...
 (S-CDE) I felt hopeful...
 (S-CDE) My life was satisfying...
 (S-CDE) My life had purpose...
 (S-CDE) My life had meaning...
 (S-CDE) I felt cheerful...
 (S-CDE) My life was worth living...
 (S-CDE) I had a sense of balance in my life...
 (S-CDE) Many areas of my life were interesting to me...
 (S-CDE) I was able to enjoy life...
 (S-CDE) I felt a sense of purpose in my life...
 (S-CDE) I could laugh and see the humor in situations...
 (S-CDE) I was able to be at ease and feel relaxed...
 (S-CDE) I looked forward with enjoyment to upcoming events...
 (S-CDE) I felt emotionally stable...

(S-CDE) I felt lovable...

(S-CDE) I felt confident...

(S-CDE) I had a good life...

(S-CDE) My life was peaceful...

(S-CDE) I was living life to the fullest...

(S-CDE) In most ways my life was close to my ideal...

(S-CDE) I had good control of my thoughts...

(S-CDE) Even when things were going badly, I still had hope...

(S-CDE) Are you able to turn a key in a lock?

(S-CDE) Are you able to brush your teeth?

(S-CDE) Are you able to make a phone call using a touch tone key-pad?

(S-CDE) Are you able to pick up coins from a table top?

(S-CDE) Are you able to write with a pen or pencil?

(S-CDE) Are you able to open and close a zipper?

(S-CDE) Are you able to wash and dry your body?

(S-CDE) Are you able to shampoo your hair?

(S-CDE) Are you able to open previously opened jars?

(S-CDE) Are you able to hold a plate full of food?

(S-CDE) Are you able to pull on trousers?

(S-CDE) Are you able to button your shirt?

(S-CDE) Are you able to trim your fingernails?

(S-CDE) Are you able to cut your toe nails?

(S-CDE) Are you able to bend down and pick up clothing from the floor?

(S-CDE) How much DIFFICULTY do you currently have using a spoon to eat a meal?

(S-CDE) How much DIFFICULTY do you currently have putting on a pullover shirt?

(S-CDE) How much DIFFICULTY do you currently have taking off a pullover shirt?

(S-CDE) How much DIFFICULTY do you currently have removing wrappings from small objects?

(S-CDE) How much DIFFICULTY do you currently have opening medications or vitamin containers (e.g., childproof containers, small bottles)?

(S-CDE) Because of my illness, some people avoided me...

(S-CDE) Because of my illness, I felt left out of things...

(S-CDE) Because of my illness, people avoided looking at me...

(S-CDE) I felt embarrassed about my illness...

(S-CDE) Because of my illness, some people seemed uncomfortable with me...

(S-CDE) I felt embarrassed because of my physical limitations...

(S-CDE) Because of my illness, people were unkind to me...

(S-CDE) Some people acted as though it was my fault I have this illness...

(S-CDE) Because of my illness, I felt embarrassed in social situations...

(S-CDE) Because of my illness, I felt emotionally distant from other people...

(S-CDE) Because of my illness, people tended to ignore my good points...

(S-CDE) Because of my illness, I was treated unfairly by others...

(S-CDE) Because of my illness, I felt different from others...

(S-CDE) Because of my illness, I worried about other people's attitudes towards me...

(S-CDE) Because of my illness, I worried that I was a burden to other...

(S-CDE) Because of my illness, people made fun of me...

(S-CDE) I was unhappy about how my illness affected my appearance...

(S-CDE) Because of my illness, strangers tended to stare at me...

(S-CDE) I lost friends by telling them that I have this illness...

(S-CDE) Because of my illness, it was hard for me to stay neat and clean...

(S-CDE) I felt embarrassed about my speech...

(S-CDE) I avoided making new friends to avoid telling others about my illness...

(S-CDE) I tended to blame myself for my problems...

(S-CDE) People with my illness lost their jobs when their employers found out about it...

(S-CDE) I am bothered by my limitations in regular family activities...

(S-CDE) I am disappointed in my ability to socialize with my family...

(S-CDE) I am bothered by limitations in my regular activities with friends...

(S-CDE) I am disappointed in my ability to meet the needs of my friends...

(S-CDE) I feel that my family is disappointed in my ability to socialize with them...

(S-CDE) I am disappointed in my ability to meet the needs of my family...

(S-CDE) I feel that my friends are disappointed in my ability to socialize with them...

(S-CDE) I am disappointed in my ability to do things for my friends...

(S-CDE) I am disappointed in my ability to socialize with friends...

(S-CDE) I am disappointed in my ability to keep in touch with others...

(S-CDE) I feel that others are disappointed in my ability to do community activities...

(S-CDE) I am disappointed in my ability to do leisure activities...

(S-CDE) I am bothered by limitations in doing my hobbies or leisure activities...

(S-CDE) I feel that I am disappointing other people at work...

(S-CDE) I am disappointed in my ability to perform my daily routines...

(S-CDE) I am disappointed in my ability to work (include work at home)...

(S-CDE) I am bothered by limitations in performing my daily routines...

(S-CDE) I am disappointed in my ability to take care of personal and household responsibilities...

(S-CDE) I am bothered by limitations in performing my work (include work at home)...

(S-CDE) I am satisfied with my ability to do things for fun outside my home...

(S-CDE) I am satisfied with the amount of time I spend doing leisure activities...

(S-CDE) I am satisfied with how much of my work I can do (include work at home)...

(S-CDE) I am satisfied with my ability to do household chores or tasks...

(S-CDE) I feel good about my ability to do things for my family...

(S-CDE) I am satisfied with my ability to meet the needs of those who depend on me...

(S-CDE) I am satisfied with my ability to do things for my family...

(S-CDE) I am satisfied with my current level of activity with family members...

(S-CDE) I am satisfied with my ability to do things for my friends...

(S-CDE) I am happy with how much I do for my friends...

(S-CDE) I am satisfied with my current level of activities with my friends...

(S-CDE) I am satisfied with the amount of time I spend visiting friends...

(S-CDE) I am satisfied with my ability to do things for fun at home (like reading, listening to music, etc.)...

(S-CDE) I am satisfied with my ability to do leisure activities ...

(S-CDE) I am satisfied with my ability to do all of the leisure activities that are really important to me...

(S-CDE) I am satisfied with my ability to do all of the community activities that are really important to me...

(S-CDE) I am satisfied with my current level of social activity...

(S-CDE) I am satisfied with my ability to run errands...

(S-CDE) I am satisfied with my ability to perform my daily routines...

(S-CDE) I am satisfied with my ability to work (include work at home)...

(S-CDE) I am satisfied with my ability to do the work that is really important to me (include work at home)...

(S-CDE) I am satisfied with my ability to take care of personal and household responsibilities...

(S-CDE) I am satisfied with the amount of time I spend doing work (include work at home)...

(S-CDE) I am satisfied with the amount of time I spend performing my daily routines...

(S-CDE) I am satisfied with my ability to work...

(S-CDE) I am bothered by limitations in performing my work...

(S-CDE) keeping track of time (eg., using a clock)?

(S-CDE) checking the accuracy of financial documents, (e.g., bills, checkbook, or bank statements)?

(S-CDE) reading and following complex instructions (e.g., directions for a new medication)?

(S-CDE) planning for and keeping appointments that are not part of your weekly routine, (e.g., a therapy or doctor appointment, or a social gathering with friends and family)?

(S-CDE) managing your time to do most of your daily activities?

(S-CDE) planning an activity several days in advance (e.g., a meal, trip, or visit to friends)?

(S-CDE) getting things organized?

(S-CDE) remembering where things were placed or put away (e.g., keys)?

(S-CDE) remembering a list of 4 or 5 errands without writing it down?

(S-CDE) learning new tasks or instructions?

(S-CDE) I made simple mistakes more easily...

(S-CDE) Words I wanted to use seemed to be on the "tip of my tongue"...

(S-CDE) I had to read something several times to understand it...

(S-CDE) I had trouble keeping track of what I was doing if I was interrupted...

(S-CDE) I had difficulty doing more than one thing at a time...

(S-CDE) I had trouble remembering whether I did things I was supposed to do, like taking a medicine or buying something I needed...

(S-CDE) I had trouble remembering new information, like phone numbers or simple instructions...

(S-CDE) I walked into a room and forgot what I meant to get or do there...

(S-CDE) I had trouble remembering the name of a familiar person...

(S-CDE) I had trouble thinking clearly...

(S-CDE) I reacted slowly to things that were said or done...

(S-CDE) I had trouble forming thoughts...

(S-CDE) My thinking was slow...

(S-CDE) I had to work really hard to pay attention or I would make a mistake...

(S-CDE) I had trouble concentrating...

(S-CDE) I had trouble getting started on very simple tasks...

(S-CDE) I had trouble making decisions...

(S-CDE) I had trouble planning out steps of a task...

Autonomic Dysfunction Following SCI Questionnaire Data Set

Was the Autonomic Dysfunction Following SCI Questionnaire Completed?

Date and Time of Data Collection

Level of Spinal Cord Injury (SCI)

If you know your severity/completeness, check one

If you know your American Spinal Injury Association Impairment Scale (AIS) grade, please check one

Please indicate any medications you are taking and dosage

If indicated Other, please specify

Amitriptyline Dosage

Baclofen Dosage

Ditropan/Oxybutinin Dosage

Gabapentin Dosage

Lyrica/Pregabalin Dosage

Midodrine Dosage

Tylenol Dosage

Dosage for medication indicated as Other

Do you have episodes of autonomic dysreflexia (AD) (a condition where blood pressure rises very fast, usually because of a painful stimulus below the level of your lesion, resulting in symptoms such as headaches, sweating, and goosebumps)?

How often does AD occur during exercise?

How often does AD occur during bladder emptying?

How often does AD occur during your bowel routine?

How often does AD occur during sexual activity?

How often does AD occur as a result of other known stimuli?

How often does AD occur spontaneously due to unknown reasons?

If you have selected 'other known stimuli', please explain (e.g. prolonged sitting):

How often do you experience headaches?

How often do you experience excessive sweating above the level of injury?

How often do you experience goosebumps?

How often do you experience anxiety?

How often do you experience heart palpitations?

How often do you experience headaches during exercise?

How often do you experience excessive sweating above the level of injury during exercise?

How often do you experience goosebumps during exercise?

How often do you experience anxiety during exercise?

How often do you experience heart palpitations during exercise?

How often do you experience headaches during bladder emptying?

How often do you experience excessive sweating above level of injury during bladder emptying?

How often do you experience goosebumps during bladder emptying?

How often do you experience anxiety during bladder emptying?

How often do you experience heart palpitations during bladder emptying?

How often do you experience headaches during your bowel routine?

How often do you experience excessive sweating above level of injury during your bowel routine?

How often do you experience goosebumps during your bowel routine?

How often do you experience anxiety during your bowel routine?
 How often do you experience heat palpitations during your bowel routine?
 How often do you experience headaches during sexual activities?
 How often do you experience excessive sweating above the level of injury during sexual activities?
 How often do you experience goosebumps during sexual activities?
 How often do you experience anxiety during sexual activities?
 How often do you experience heart palpitations during sexual activities?
 How often do you experience headaches due to other known stimuli?
 How often do you experience excessive sweating above the level of injury due to other known stimuli?
 How often do you experience goosebumps due to other known stimuli?
 How often do you experience anxiety due to other known stimuli?
 How often do you experience heart palpitations due to other known stimuli?
 Please rate how headaches affect you during daily living
 Please rate how sweating above the level of injury affects you during daily living
 Please rate how goosebumps affect you during daily living
 Please rate how anxiety affects you during daily living
 Please rate how heart palpitations affect you during daily living
 Please rate how headaches affect you during exercise
 Please rate how sweating above the level of injury affects you during exercise
 Please rate how goosebumps affect you during exercise
 Please rate how anxiety affects you during exercise
 Please rate how heart palpitations affect you during exercise
 Please rate how headaches affect you during sexual activity
 Please rate how sweating above the level of injury affects you during sexual activity
 Please rate how goosebumps affect you during sexual activity
 Please rate how anxiety affects you during sexual activity
 Please rate how heart palpitations affect you during sexual activity
 How often do you experience dizziness during the day?
 How often do you experience light headedness during the day?
 How often do you experience blurred vision during the day?
 How often do you experience nausea during the day?
 How often do you experience weakness during the day?
 How often do you experience confusion during the day?
 How often do you experience fatigue during the day?
 How often do you experience passing out during the day?
 What usually triggers these symptoms (e.g. heat, change in position)?
 How often do you experience dizziness during transfers from the bed to your wheelchair?
 How often do you experience light headedness during transfers from the bed to your wheelchair?
 How often do you experience blurred vision during transfers from the bed to your wheelchair?
 How often do you experience nausea during transfers from the bed to your wheelchair?
 How often do you experience weakness during transfers from the bed to your wheelchair?
 How often do you experience confusion during transfers from the bed to your wheelchair?
 How often do you experience fatigue during transfers from the bed to your wheelchair?
 How often do you experience passing out during transfers from the bed to your wheelchair?
 How often do you experience dizziness after a meal?
 How often do you experience light headedness after a meal?
 How often do you experience blurred vision after a meal?
 How often do you experience nausea after a meal?
 How often do you experience weakness after a meal?
 How often do you experience confusion after a meal?
 How often do you experience fatigue after a meal?
 How often do you experience passing out after a meal?
 How often do you experience dizziness during or after exercise?
 How often do you experience light headedness during or after exercise?
 How often do you experience blurred vision during or after exercise?
 How often do you experience nausea during or after exercise?
 How often do you experience weakness during or after exercise?

How often do you experience confusion during or after exercise?
How often do you experience fatigue during or after exercise?
How often do you experience passing out during or after exercise?
Please rate how dizziness affects you during transfers
Please rate how light headedness affects you during transfers
Please rate how blurred vision affects you during transfers
Please rate how nausea affects you during transfers
Please rate how weakness affects you during transfers
Please rate how confusion affects you during transfers
Please rate how fatigue affects you during transfers
Please rate how passing out affects you during transfers
Please rate how dizziness affects you after a meal
Please rate how light headedness affects you after a meal
Please rate how blurred vision affects you after a meal
Please rate how nausea affects you after a meal
Please rate how weakness affects you after a meal
Please rate how confusion affects you after a meal
Please rate how fatigue affects you after a meal
Please rate how passing out affects you after a meal
Please rate how dizziness affects you during or after exercise
Please rate how light headedness affects you during or after exercise
Please rate how blurred vision affects you during or after exercise
Please rate how nausea affects you during or after exercise
Please rate how weakness affects you during or after exercise
Please rate how confusion affects you during or after exercise
Please rate how fatigue affects you during or after exercise
Please rate how passing out affects you during or after exercise
Conditions under which orthostatic conditions occur
Standing/Sitting Time
Is there anything that was not asked that you would like us to know?